

# Department of Clinical Investigation Annual Research Progress Report



**Fiscal Year 2002**  
Madigan Army Medical Center  
Tacoma, Washington

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## **APR FY 02 Errata**

Protocol #: 202/016

Title: Evaluation of Fecal Lactoferrin Levels of Inflammatory Bowel Disease and Irritable Bowel Syndrome Patients

Department: Incorrectly listed as Medicine/Gastroenterology should be Pathology

Protocol #: 202/080

Title: The Fate and Therapeutic Impact of Exogenous Type II Pneumocytes in B6129SF2/J Mice

Department: Surgery/General Surgery should be Clinical Investigation

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**ANNUAL PROGRESS REPORT**

30 SEPTEMBER 2002

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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**FISCAL YEAR 2002**  
**DEPARTMENT OF CLINICAL INVESTIGATION**  
**MADIGAN ARMY MEDICAL CENTER**  
**TACOMA, WASHINGTON 98431**

**Introduction**

In conducting the research described in this report, the investigators adhered to the “Guide for the Care and Use of Laboratory Animals” as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

**Acknowledgments**

I would like to take this opportunity to thank Barbara Jones, Troy Patience, Paul Froude, Genie Hough, Mary Porreca and Tammie Maple for their effort, in the compilation, preparation, and editing of this publication.

## **Foreword**

2002 was a year of major growth and change in the Madigan Department of Clinical Investigation (DCI). Dr. Curtis Yeager (LTC(ret), MS, USA) was added as Chief, Research Administration Service and Dr. Patrick McNutt (CPT, MS, USA) is the new Chief, Research Operations Service.

Despite a large turnover in Graduate Medical Education (GME) program leadership, and a marked increase in deployments secondary to the world situation, we again saw an increase in scholarly activity at Madigan. The DCI supported 430 research protocols during the year, of which 141 were new protocols.

The very important GME mission at Madigan continues to receive strong support from the DCI through leadership in curriculum development, medical education, research facilitation, and the unique training opportunities available through our department infrastructure (e.g. PALS and ATLS courses, combat trauma management training, advanced laparoscopic surgery training, molecular biotechnology techniques courses, etc.). Additionally, the OB/GYN Department, in collaboration with the DCI and University of Washington, initiated an objective surgical skills assessment program to monitor resident progress throughout their training.

DCI leaders continued their outreach program to MAMC Departments, teaching the regulatory requirements for ethical conduct of research, and continuing special emphasis on military unique medical research and training. More than 50 residents, fellows, and faculty participated in this year's "Introduction to Clinical Research Short Course," which will be offered twice next year. The DCI also provided pre-review and design support to MAMC medical executives seeking to improve the quality of patient care through a more scientific approach to managed care. In addition, the General Surgery Residency assigned CPT Phillip Mullenix to DCI for a year rotation. This highly successful collaboration is on the heels of our first resident CPT Rebecca McGuigan.

Madigan Research Day 2002 (MRD 2002) was held on 26 April 2002, and once again provided an outstanding forum for showcasing the scope and vigor of multi-service (USA, USAF, USN, USCG) scholarly activity and clinical research conducted at our medical center, and within our region. Sixty-seven abstracts were submitted and reviewed by subcommittees, with 25 selected for podium presentations, and 28 presented as posters. The presentations focused on research efforts in the areas of Military Unique Clinical Investigation, Scientific Approach to Managed Care, Medical Education, Experimental Design, and Case Reports. The day was greatly refined and supported through the generous sponsorship of the COL Patrick S. Madigan, Geneva, and Henry M. Jackson Foundations.

### **Madigan Research Day 2003 will be held on 25 April 2003**

#### ***Research Administration Service (RAS)***

The RAS changed leadership several times this past FY, starting with interim chiefs, Mr. Jeff Bullock (OCT 01) and Ms. Barbara Jones (NOV 01-FEB 02), to the current chief, Dr. Curtis Yeager (FEB 02). Ms. Mary Porreca joined the staff as the new Research Protocol Clerk and was immediately instrumental in the retirement and physical relocation of some 30 years of MAMC research records.

As an institutional activity, the MAMC IRB and its policies and procedures continued to evolve to ensure compliance with the ever-expanding requirements for documented protection of human subjects. The MAMC IRB was registered with the Office of Human Research Protections and awarded the new Federal-Wide Assurance. In accordance with the FWA, the IRB implemented new training requirements for all research personnel. The required training can be obtained either by completion of a comprehensive web-based program subscribed with the University of Miami or the DCI-sponsored Introduction to Clinical Research Course, which is presented in conjunction with the MAMC Faculty Development Fellowship and held semi-annually. The RAS continues to develop and implement new policies and procedures for IRB functions to maximize compliance with all relevant federal requirements. Of note, a new intranet, web-based system for pre-IRB

review of protocols was implemented and provides a platform for the early detection and resolution of protocol issues, saving valuable convened IRB time. The IRB underwent External Audits by the AMEDDC&S Clinical Investigation Regulatory Office and the Southwest Oncology Group, both with favorable results, thanks to the professional efforts of the combined MAMC research staff, but particularly the DCI Protocol Specialist, Ms. Barbara Jones.

As the FY closes, RAS plans to: (1) complete the development of extensive local written guidance for the IRB and WRMC researchers; (2) enter a Quality Assurance and Improvement liaison with OHRP to enhance human subjects protection and ensure institutional compliance and excellence; and, (3) to acquire additional staff to develop and implement an Internal Research Audit Program and to improve IRB efficiency and decrease turn around times.

### ***Laboratory Animal Resources Service***

The LARS supported two Advance Trauma Life Support courses and there Pediatric Life Support courses for Madigan Army Medical Center. In addition, specifically requested by unit surgeons, LARS conducted two separate, animal-based, combat trauma management training exercises in a field setting. The two exercises challenged the trauma management skills of personnel from one Army Forward Surgical Team and all Ranger medics from the 2/75 Ranger Battalion. The other exercise consisted of seven operational detachments from the 2<sup>nd</sup> Battalion, 1<sup>st</sup> Special Forces Group in conjunction with the 54<sup>th</sup> Medical Company, Air Ambulance. Specifically requested by unit surgeons, these two exercises filled training gaps with all units involved and greatly enhanced their medical readiness. As the FY closes, LARS is preparing for their upcoming Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) inspection scheduled third quarter of calendar year 2003

### ***Research Operations Service***

The ROS continued their hard work from last year, immersed in sixteen basic research protocols ranging from infection of dystrophin-null mice with a MyoD-expressing retrovirus to exploring the molecular mechanisms underlying acute respiratory distress syndrome. We are involved in collaborations with researchers around the country studying the endothelial contribution to preeclampsia and the molecular epidemiology of disease vectors in Central America as well as providing technical assistance as necessary to the burgeoning molecular diagnostics branch of the Department of Pathology. In the past year, our functional potential increased substantively with the acquisition of two high-throughput DNA sequencers, a top-of-the-line image analysis workstation, and the in-house ability to analyze microchip gene arrays. The ROS staff is starting several basic science research protocols utilizing cutting-edge molecular and cellular techniques to:

- Design and test a botanical protein expression system for oral vaccines, biopharmaceuticals, and phytoremediation protocols;
- Design a real-time PCR analysis to identify causative agents of chorioamnionitis;
- Explore the potential of using small inhibitory RNAs to reverse drug resistance in cancer cell lines;
- Utilize adenoviral, retroviral and lentiviral vectors to modify cultured and primary cell lines to explore aspects of gene expression.

Participating in these ROS-initiated protocols will provide MAMC investigators with practical experience in a basic research environment, illustrating the power and limitations of modern molecular, biology, the relationship between basic research and clinical research and exposing them to new research technologies to support the clinical investigations.

In all, 2002 was a very exciting and productive year for clinical research at MAMC, and for the DCI. We remain vigorously committed to quality and compliant clinical investigation, and we deeply appreciate the collegial collaboration opportunities that we enjoy with other military and civilian medical centers, Departments of Clinical Investigation, and with the Clinical Investigation Regulatory Office at the AMEDD Center & School.



## UNIT SUMMARY - FISCAL YEAR 2002

### A. Objective:

Provide and create an environment to support clinical and basic medical research within Madigan Army Medical Center. Clinical Investigation exists to further the highest degree of medical readiness. DCI supports the Graduate Medical Education mission through leadership in curriculum development, medical education research, and military unique clinical investigations, as well as training opportunities available through institutional programs (ATLS, PALS, etc.)

### B. Technical Approach:

All research, investigational and training activities within the Department of Clinical Investigation are conducted under the guidance of the office of Human Research Protections (OHRP), FDA, AR 40-7, AR 40-38, AR 70-25, and AR 70-18. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

### C. Staffing:

| <u>Name</u>            | <u>Rank</u> | <u>MOS</u> | <u>Title</u>                 |
|------------------------|-------------|------------|------------------------------|
| Ricks, Robert E        | COL         | 60J9B      | Chief, DCI                   |
| Maple, Tammie          | GS11        | 0671       | Administrative officer       |
| Patience, Troy         | GS11        | 1530       | Statistician (Medicine)      |
| Hough, Eugenia         | GS06        | 0318       | Secretary/Steno              |
| Norlund, Lewis L.*     | MAJ         | 75C64      | Chief, Lab Animal Res Svc    |
| Gibson, Steven         | SFC         | 91T4H25    | NCOIC, DCI                   |
| Sanchez, Michael       | SGT         | 91T10      | Animal Care Specialist       |
| Criss, Amy             | SPC         | 91T10      | Animal Care Specialist       |
| Montminy, Timothy      | PFC         | 91T10      | Animal Care Specialist       |
| Spahn-Bridges, Shelley | WG05        | 5048       | Animal Caretaker             |
| McNutt, Patrick        | CPT         | 71B        | Chief, Research Op Svc       |
| Bullock, Jeff          | GS11        | 0644       | Medical Technologist         |
| Matej, Louis           | GS11        | 0644       | Medical Technologist         |
| DeHart, Mary           | GS11        | 0644       | Medical Technologist         |
| Wright, James          | GS11        | 0644       | Medical Technologist         |
| Yeager, Curtis         | GS13        | 0601       | Chief, Research Admin Svc    |
| Jones, Barbara         | GS09        | 0301       | Research Protocol Specialist |
| Froude, Paul           | GS07        | 0303       | Research Protocol Assistant  |
| Porreca, Mary          | GS05        | 0303       | Research Protocol Clerk      |

\*ETS'd in August 2002

| Personnel: | <u>Authorized**</u> | <u>Required**</u> | <u>Assigned</u> |
|------------|---------------------|-------------------|-----------------|
| Officers-  | 5                   | 8                 | 3               |
| Civilians- | 8                   | 15                | 12              |
| Enlisted-  | 8                   | 9                 | 4               |

\*\*IAW ASAM I and FY02 Optimization

## D. Funding:

### FY02 Research Resources

#### P8 Funds

|  |                  |
|--|------------------|
| Civilian Payroll (includes overtime - \$5,866) | \$676,953        |
| Incentive Awards                               | \$ 2,310         |
| Operations                                     | \$102,983        |
| CEEP (Ultra low freezer)                       | \$ 7,700         |
| TDY (CHE)                                      | \$ 2,121         |
| TDY for researchers to present                 | \$ 36,351        |
| Reproduction Requests                          | \$ 568           |
| Contracts                                      | \$ 515           |
| MEDCASE (Image Analysis)                       | \$116,000        |
| Military Payroll (est.)                        | <u>\$411,338</u> |

**\$1,356,839**

#### MAMC Resource Management Division Oversight

|   |                  |
|---|------------------|
| Military Interdepartmental Purchase Request (MIPR~) | \$2,187,547      |
| Lab Animal Training protocols MIPR                  | \$ 7,460         |
| MAMC (CRDA, Protocol 201139**)                      | <u>\$ 10,850</u> |

**\$2,205,857**

#### Grants Federal

|   |                  |
|---|------------------|
| Henry M. Jackson Foundation (USUHS)         | \$ 11,900        |
| The Geneva Foundation (Tri-Service Nursing) | \$208,066        |
| Patrick S. Madigan Foundation (SWOG*)       | \$ 12,413        |
| Children's Oncology Group (COG*)            | <u>\$ 23,836</u> |

**\$256,215**

#### Grants Nonfederal

|                                    |                  |
|------------------------------------|------------------|
| Henry M. Jackson Foundation (CRDA) | \$ 97,600        |
| The Geneva Foundation (CRDA)       | \$197,158        |
| Nonfederal Education Grants        | <u>\$320,906</u> |

**\$615,664**

### FY02 Research Resources Total

**\$4,434,575**

\* NIH original source of funds distributed via Southwest Oncology Group & Swedish Medical Center, Seattle WA. COG and SWOG are treated as federal sources IAW AR 40-38, para 3-6, b. 3(f).

\*\* MPMC original source of funds distributed via CRDA with Oregon Laser, Portland, OR.

~ Protocols 201131, 202113, 200117

## **E. Progress**

During FY 2002, there were 429 active protocols that received administrative and/or technical support during the year. of these, 292 are presently ongoing, none are in a suspended status, 72 were completed, and 30 were terminated. The principal investigator distribution was as follows: 296 staff protocols, 78 resident protocols, 14 fellow protocols, 2 intern protocols, and 1 Weed Army Community Hospital protocol. There were 123 new protocols.

There were 68 publications in nationally recognized journals and 60 presentations at regional or national medical association meetings.

## **F. Fellowship/Residency Program Support**

**Programs supported by DCI:** 21 residencies and 5 fellowships, they are:

*Residencies:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Occupational Therapy, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Pediatric Psychology, Pharmacy, Physician Assistance Program (Emergency Medicine & Orthopaedics), Podiatry, Preventive Medicine (Public Health), Radiology, Transitional Year, and Urology.

*Fellowships:* Developmental Pediatrics, Faculty Development (Family Practice), Geriatrics, Maternal-Fetal Medicine, and Urogynecology.

19 protocols involving 90 residents

66 protocols involving 5 fellows

### **Other training programs supported by DCI:**

DCI: 200/073, 200/146

Department of Surgery: 201/091, 99/087, 99/050, 202/025

Department of Emergency Medicine: 202/093

Department of Pediatrics: 201/142

## **G. Committee Members**

### Clinical Investigation Committee

COL Robert E. Ricks, MC

Chairman

Chief or delegated representative of:

Department of Anesthesia and Operative Services

Department of Emergency Medicine

Department of Family Practice

Department of Medicine

Department of Medicine, Cardiology Service

Department of Nursing

Department of OB/GYN

Department of Pathology

Department of Pediatrics

Department of Radiology

Department of Surgery

Department of Surgery, Orthopedics Service

Pharmacy Service

Physical Medicine & Rehabilitation Service

Preventive Medicine Service

Department of Clinical Investigation (DCI)

Clinical Studies Service, DCI

Medical Statistician, DCI

Research Administration Service, DCI

Research Operations Service, DCI

Research Operations Service, Microbiology Section, DCI

Human Use Committee  
COL Robert E. Ricks, MC  
Chairman

Chief or delegated representative of:

- Department of Alternate Chairperson
- Department of Nursing
- Department of Pediatrics
- Department of Radiology
- Department of Ministry and Pastoral Care
- Department of Clinical Investigation
- Research Administration Service, DCI
- Pharmacy Service
- Social Work Service
- Center Judge Advocate
- Non-institutional Member

Animal Use Committee  
COL Jerome Myers, MC  
Chairman

Chief or delegated representative of:

- Department of Clinical Investigation (DCI)
- Department of Pathology
- Department of Medicine
- Department of Surgery
- Northwest Veterinary Service Support Area
- Non-affiliated Member and Alternate Non-affiliated Member
- Attending Veterinarian, DCI
- Animal Care Worker, DCI

## **H. Awards**

### **Steger Award**

This award is given to a resident, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2002: *CPT Leroy T. Trombetta, MC for his paper entitled "A Quantitative Assay for Telomerase Enzyme Activity Predicts Severity of Disease in Neuroblastoma"*

### **COL Patrick S. Madigan Foundation Research Award**

This award is given to a fellow, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2002: *MAJ Christine M. Kovac, MC for her paper entitled "Maternal Ethnicity and Second-trimester Fetal Femur Length Variation"*

### **Kenyon Joyce Award**

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2002: *LTC Byron C. Calhoun, MC for his paper entitled "Multifetal Pregnancies: Evolution of Methods of Initiation and Impact of REI Certification for Patients Seeking Reduction"*

## **Madigan Research Day Awards**

This award is given during Madigan's Annual Madigan Research Day to recognize the best presentation in the following four categories: Innovation, Change in Practice, Interdisciplinary, and Discovery. This year's winners are:

### ***INNOVATION AWARD***

**Presented to:** CPT Rebecca McGuigan, MC

**Department:** Surgery/General Surgery Service

**Title:** Development of an ARDS Model using Oleic Acid in the Laboratory Rat

**Mentor:** COL Robert Ricks, MC

### ***CHANGE IN PRACTICE AWARD***

**Presented to:** LTC Joan K. Vanderlaan, AN

**Department:** ROTC Regional HQ

**Title:** Weight and Body Fat Percentage Gain or Loss at ROTC Advanced Camp 2000

**Mentor:** COL Eileen Hemman, AN

### ***INTERDISCIPLINARY AWARD***

**Presented to:** CPT Thomas L. Sutton, MC

**Department:** Pediatrics

**Title:** Intraprevalence of Chlamydia Trachomatis in Male College ROTC Cadets

**Mentor:** LTC Mary P Fairchok, MC

### ***DISCOVERY AWARD***

**Presented to:** CPT Dean R. Focht III, MC

**Department:** Pediatrics

**Title:** The Efficacy of Duct Tape versus Cryotherapy in the Treatment of Verruca Vulgaris (the Common Wart)

**Mentor:** LTC Mary P. Fairchok, MC

### ***BG GEORGE J. BROWN MENTOR'S CUBE***

**Presented to:** COL Joe Yetter, MC

**Department:** Family Practice

### ***NANCY J. WHITTEN OUTSTANDING IRB MEMBER AWARD***

**Presented to:** LTC Kenneth Azarow, MC

**Department:** Surgery/General Surgery Service

### ***BG MACK C. HILL FACILITATOR'S AWARD***

**Presented to:** Tom Pierce

**Department:** Educational Resources/Medical Illustration Service

## **I. Presentations**

### **Department of Clinical Investigation**

Ricks RE. Female Soldier Readiness Medical Readiness for Female Soldiers, a MAMC/I Corps Partnership. Presented at Armed Forces District Annual Meeting, Norfolk, VA.

Ricks RE, Hume RF, Walker WO, Kelly P, Chow G, Peterson C, Della-Guisina K, Calhoun BC. Mentoring Mentors: (MAPS) Enhanced Scholarly Activity Through Management of Mentor and Protege Synergy. Presented at APGO/CREOG, Dallas, TX.

Jones JM. Prevention of Hypertension (HTN) in the United States Army: A Descriptive Correlational Study of the Dietary Habits of Enlisted Soldiers, Ft Lewis, WA. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, April 2002.

### **Department of Family Practice**

Padden MO, Lim M. Graduate Medical Education and Family Medicine: What Do Young Family Physicians Value Regarding Residency Training Curriculum? Presented at Society for Teachers of Family Medicine, San Francisco, CA, USA, April 2002.

Rosen IM, Krueger MV. Prenatal Breastfeeding Education: Determining the Most Effective Method. Presented at Uniformed Services Academy of Family Practice, Orlando, FL, USA, March 2002.

Barrett JP, Flynn DM. Awareness and Acceptance of Emergency Contraception Among Female Soldiers and Wives of Soldiers at Fort Lewis, Washington. Presented at Society of Teachers of Family Medicine Annual Spring Conference, San Francisco, CA.

O'Boyle AL, Krueger MV, Davis G. Teaching and Evaluation of Procedural Skills in the Repair of Episiotomy and Obstetrical Lacerations. Presented at The Society of Teachers of Family Medicine, San Francisco, CA.

### **Department of Nursing**

Brosch LR, Loan LA, Hemman EA, Patrician PA. Standardizing and Comparing Nurses' Perception and Patient Falls Data at Two Army Medical Centers. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, USA, April 2002.

Anderson RA, Allred CA, Jacques RC, Hunt EC, Turner L. Risk Factors and Chronic Disease Profile of Active Duty Soldiers. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, USA, April 2002.

Loan LA, Miltner R, Ruiz E, Mittelstaedt E. Postpartum HCT: Using Evidence to Change Practice. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, USA, April 2002.

Brosch LR, Miltner RS, Loan LA, Jennings BM. Predictors of Potentially Preventable Hospitalization in Older Healthcare Beneficiaries Enrolled in a Military Medicare Subvention Demonstration. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, April 2002.

Brosch LR, DePaul D, Forsythe M, Loan LA. Factors Associated with Physical Activity and Exercise in Active Duty Female Soldiers. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, April 2002.

Brosch LR, Miltner RS, Loan LA, Jennings BM. TRICARE Senior Prime Beneficiaries: They Aren't Who We Thought They Would Be. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, April 2002.



Jennings BM, Loan LA. Expectations of Military Health Care: An Inductive Analysis. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, April 2002.

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Jones JM, Bice-Stephens WM. Prevention of Hypertension (HTN) in the United States Army: A Descriptive Correlational Study of the Dietary Habits of Enlisted Soldiers, Ft Lewis, Washington. Presented at 12th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, USA, May 2002.

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Brosch LR, Miltner RS, Loan LA, Jennings BM. TRICARE Senior Prime Beneficiaries: They Aren't Who We Thought They Would Be. Presented at Karen A. Reider Nursing Research Poster Session at AMSUS 108th Annual Meeting, San Antonio, TX, USA, November 2001.

Simon SR, Mittelstaedt EA. Implementation of a Car Seat Safety Program. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, USA, April 2002.

Vanderlaan JK. Weight and Body Fat Percentage Gain or Loss at ROTC Advanced Camp 2000. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, USA, May 2002.

Cherry JP, Wilson FH, Hill EE, Hall JA, Hachey MD. Postoperative Pain Following Psoas Compartment Block with General Anesthesia as Compared to Subarachnoid Block for Total Knee Arthroplasty. Presented at The American Association of Nurse Anesthetists, Orlando, FL, August 2002.

Kerkenbush NL. Implementation of a Diabetic Disease Management Program. Presented at 12th Annual Summer Institute in Nursing Informatics, Baltimore, MD, USA, July 2002.

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Parker JD, Nielsen PE, Troop D. The Effect of a Prepared Study Guide by Residents as a Tool to Improve CREOG Scores. Presented at APGO/CREOG, Dallas, TX.

### **Department of Pathology**

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### **Department of Pediatrics**

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### **Cardiothoracic Service, Department of Surgery**

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### **General Surgery Service, Department of Surgery**

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### **Cardiology Service, Department of Medicine**

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### **Northwest Lead Agent**

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### **Otolaryngology Service, Department of Surgery**

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## K. Exempt Protocols

| <b>Number</b> | <b>Prin. Investigator</b> | <b>Title</b>   |
|---------------|---------------------------|--|
| 202/111       | Arcila ME                 | A Comparison of Diagnostic Yield of Routine Cytologic Cell Block Preparations Obtained by Fine Needle Aspirations  |
| 202/076       | Barrett JP                | Factors Associated with Intentions to Leave the Army when Pregnant. (Secondary analysis of pre-collected data from MAMC protocol #97050: Unintended Pregnancy Prevention Program, by LTC Jeffery Clark, then LTC Dianne Flynn, Principal Investigator) |
| 202/019       | Barrett JP                | Awareness and Acceptance of Emergency Contraception Among Female Soldiers and Wives of Soldiers at Fort Lewis, Washington  |
| 202/034       | Bullock JM                | Expression of Angiostatin and TSP1 in Human Microvascular Endothelial Cells and Breast Cancer Cells: In Vitro Study of a Potentially Superior Antiangiogenic Activity  |
| 202/001       | Calhoun BC                | Natural History of Intrauterine Fetal Demise (IUFD) in Twin Gestation  |
| 202/052       | Cavicchia MA              | Missed Opportunities for Pneumococcal Vaccination in Adults with Chronic Disease   |
| 202/035       | Chalmers RW               | An Evaluation of Hematocrit as a Screening Test Used in the Diagnosis of Ectopic Pregnancy   |
| 202/110       | Chalmers RW               | Predictors of Performance on the In-service Examination in Obstetrics and Gynecology   |
| 202/037       | Compton K                 | Bowel Frequency Normals in 0 to 4 Month Infants and Parental Perception of Constipation  |
| 202/017       | Cosio EN                  | Quality Improvement Project: A Needlestick Prevention Program  |
| 202/038       | Cuenca PJ                 | Intubating Laryngeal Mask Airway versus Laryngoscopy and Endotracheal Intubation in the Special Operations Environment   |
| 202/042       | Foglia LM                 | Assessment of an Introductory Training Program for New Residents Including Evaluation of Episiotomy Repair Skills  |
| 202/079       | Hurtado TR                | Emergency Department Treatment of Migraine Headache: Factors Influencing Clinician Preferences   |
| 202/020       | Otto CS                   | The Use of Wavefront Technology to Measure Accomodative Amplitude  |
| 202/021       | Padden MO                 | Evaluation of the Family Medicine Integration Project  |
| 202/004       | Parker JD                 | The Effect of a Prepared Study Guide by Residents as a Tool to Improve CREOG Scores  |
| 202/040       | Plummer AD                | Association of Medical Profile and Body Mass Index   |
| 202/018       | Serna ED                  | A Continuous Quality Improvement Project to Examine and Enhance Nurse's Management of Tube Feedings  |
| 202/024       | Tillotson-Criss MC        | Tick Surveillance and Analysis for <i>Borrelia burgdorferi</i> and the Human Granulocytic Ehrlichiosis Agent in Pierce County, Washington  |

## L. Detail Summary Sheet – Table of Contents

Detail Summary Sheets

Legend: St = Status [Categories: O – Ongoing, C – Completed, T – Terminated]

| <b><u>Prin. Invest.</u></b>                 | <b><u>St</u></b> | <b><u>Title</u></b>  | <b><u>Page</u></b> |
|---|------------------|--|--------------------|
| <b><u>Protocol #</u></b>                    |                  |  |                    |
| <b>DEPARTMENT OF CLINICAL INVESTIGATION</b> |                  |  | <b>47</b>          |
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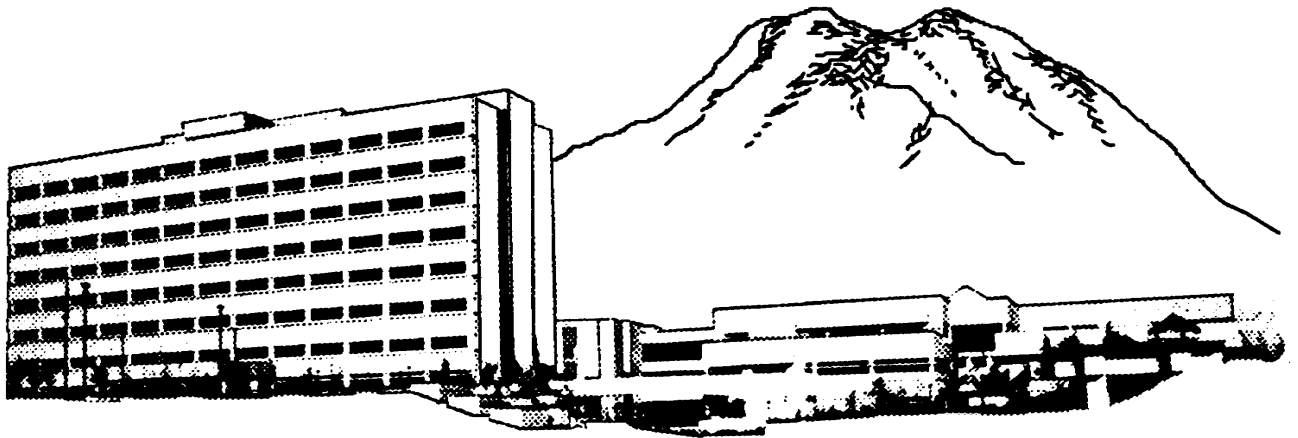
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| Lance RS<br>#202/046                                    | O                | A Randomized Trial of Radical Prostatectomy versus Brachytherapy for Patients with T1c or T2a N0 M0 Prostate Cancer  | 449                |
| Lance RS<br>#98/114                                     | T                | A Uniformed Services Comprehensive Database and Tissue Repository for the Study of Epidemiological, Detection, Natural History, and New Management Strategies for Prostate Cancer  | 450                |
| Lance RS<br>#202/090                                    | O                | An Open-Label Trial on the Effect of I.V. Zometa 4 mg on Bone Mineral Density in Hormone Sensitive Prostate Cancer Patients with Bone Metastasis, Protocol Number CZOL446EUS24   | 451                |

| <b><u>Prin. Invest.</u></b><br><b><u>Protocol #</u></b> | <b><u>St</u></b> | <b><u>Title</u></b>   | <b><u>Page</u></b> |
|---|------------------|---|--------------------|
| Lance RS<br>#201/140                                    | O                | Intratumoral Treatment of Human Prostate Cancer Xenografts by Polymeric Gel Delivery of Yttrium-90 with and without Taxol   | 452                |
| Lance RS<br>#98/092                                     | O                | Multicenter Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analysis   | 453                |
| Lance RS<br>#94/010                                     | O                | SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup   | 454                |
| McMann LP<br>#202/122                                   | O                | Followup of Testicular Microlithiasis in an Asymptomatic Population   | 455                |
| McMann LP<br>#202/065                                   | O                | Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial  | 456                |
| McMann LP<br>#201/069                                   | O                | Outcome After Ureteral Reimplantation: A Comparison of Extravesical Versus Intravesical Techniques, A Retrospective Study   | 457                |
| McMann LP<br>#201/066                                   | C                | Significance of Soluble Fas in the Serum of Patients with Prostate Cancer   | 458                |
| Poulton TL<br>#200/060                                  | C                | The Effect of 1,25-dihydroxyvitamin D3 (vitamin D) on Vascular Endothelial Growth Factor (VEGF) mRNA and Protein Expression in Prostate and Bladder Cancer Cell Lines   | 459                |
| <b>VASCULAR SURGERY, DEPARTMENT OF SURGERY</b>          |                  |   | <b>460</b>         |
| Andersen CA<br>#202/070                                 | O                | A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy with Split-Thickness Skin Grafting in the Treatment and Blinded Evaluation of Venous Stasis Ulcers, Protocol Number VAC2001-03 | 461                |
| <b>WEED ARMY COMMUNITY HOSPITAL</b>                     |                  |   | <b>462</b>         |
| Potter MB<br>#202/104                                   | O                | Coccidioidomycosis Seroincidence Study  | 463                |





## **Detail Summary Sheets**

### **Department of Clinical Investigation**

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/026      **Status:** Ongoing

**Title:** Differential mRNA Expression in the Preeclamptic vs. Normal Human Placenta

**Principal Investigator:** M. J. DeHart, B.S.

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** CPT Robert L. Behrman, MC; MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; Laura S. Martin, M.D.; MAJ Bobby C. Howard, MC, USAF; MAJ Christine M. Kovac, MC; CPT Patrick M. McNutt, MS

**Keywords:** differential gene expression, preeclampsia, cDNA expression arrays, placenta

**Start Date:**  
11/28/2000

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
11/27/2001

**Study Objective:** To identify genes differentially expressed in placentas from patients with preeclampsia compared to placentas from normal pregnancies.

**Technical Approach:** Prospective case-controlled observational study with placental tissue collection. Placental samples will be collected immediately after delivery and rinsed in physiological saline. The basal plate (cotyledon) excluding the large vessels will be sectioned into approximately 0.5 g pieces, snap frozen in liquid nitrogen, and stored at -70°C until mRNA analysis. Maternal age, gestational age at delivery, and birth weight will be recorded for each placenta. An anonymously coded clinical data sheet will be used to identify cases and controls. Differential gene expression: Placental tissue from a preeclamptic patient and a normal pregnancy will undergo differential gene expression analysis using the Atlas™ cDNA Expression Array technology (Atlas™ Custom Hybridization and Analysis Service, Clontech, Palo Alto, CA). Frozen specimens (approximately 0.5 g tissue each from one preeclamptic placenta and one normal placenta) will be mailed to Clontech for analysis. RNA will be isolated from these placental samples, and cDNA probes will be prepared using a gene-specific primer mix and hybridized to a nylon array of 1,176 human genes involved in a wide range of biological pathways. Computer analysis of phosphorimages by Clontech's AtlasImage™ software will compare expression signals to generate a gene expression profile mailed to us by Clontech. Differential expression of identified genes will be confirmed at the Department of Clinical Investigations Laboratory via Northern analysis (below) if cDNA probes are available. If cDNA probes cannot be obtained, reverse transcriptase polymerase chain reaction (RT-PCR) using gene-specific PCR primers obtained from Clontech will be performed using PCR conditions as per the manufacturer's instructions. This analysis to confirm differential expression will be performed on 10-25 placentas from pregnancies complicated by preeclampsia and 10-25 placentas from normal pregnancies, including tissue from the placentas used to obtain the original gene expression profile. Of note is that this is not considered a genetic study because we are not linking the results to the family. This study is for research purposes only. Patients will not be contacted with their differential expression profiles.

Northern analysis: Total cellular RNA will be isolated from the placental tissue using the method of Chomczynski and Sacchi (26). Frozen tissues will be placed into 3 ml of Solution D (26) in a 50 ml tube on dry ice and will be minced with a scalpel. Samples will then be homogenized at room temperature with a Polytron hand-held tissue homogenizer and allowed to sit at room temperature for 15 min. One-tenth volume of 2M sodium acetate (pH 4.0), one-fifth volume of chloroform-isoamyl alcohol mixture (48:1), and an equal volume of diethyl pyrocarbonate (DEPC)-treated water-saturated phenol will be added to each homogenate with thorough mixing by inversion after the addition of each reagent. The final suspension will be shaken vigorously, transferred to a 15 ml tube, and cooled on ice for 20 min. Samples will be centrifuged at 4°C for 20 min. at 9,500 rpm in a Beckman GS-15R tabletop centrifuge. The aqueous layer will be removed and placed into 1.5 ml microcentrifuge tubes in 600 µl aliquots. An equal volume of isopropanol will be added and samples will either be frozen overnight at -70°C or on dry ice for 15 min. Samples will be

centrifuged at 15,300 rpm for 20 min., and the resulting RNA pellets will be dissolved in 600 ml of Solution D, precipitated again with an equal volume of isopropanol either overnight at -70°C or on dry ice for 15 min., centrifuged for 20 min., and washed in 80% ice cold ethanol. RNA pellets will be centrifuged for 10 min., resuspended in 75 ml DEPC-treated water, and quantitated using a UV spectrophotometer.

Total RNA (30 mg/lane) will be denatured, resolved in a 1.2% agarose-formaldehyde gel, transferred to a GeneScreen (NEN, Boston, MA) membrane in 10X saline sodium citrate (SSC), and UV cross-linked to the membrane. Probes will consist of complementary DNAs for differentially expressed genes identified by hybridization with the Atlas™ cDNA Expression Arrays (Clontech, Palo Alto, CA) and 18S ribosomal RNA (Ambion, Inc., Austin, TX) as an internal loading standard. Probes will be labeled by random priming (Amersham, Arlington Heights, IL) with [ $\alpha$ -32P]dCTP (3000 Ci/mmol, Amersham, Arlington Heights, IL) and the Klenow fragment of E. coli DNA polymerase. Unincorporated counts will be removed using STE push columns (Stratagene, La Jolla, CA). Prehybridization and hybridization will be performed at 55°C using the Super™ Hybridization Buffer System (DNA Technologies, Inc., Rockville, MD) following the manufacturer's instructions. Blots will be washed 3 x 5 min. in 2X SSC at room temperature before images will be obtained with a BioRad GS-505 Molecular Imager System. Blots which will be stripped and reprobbed with the 18S complementary cDNA will be washed in the buffers supplied in the Super™ Hybridization Buffer System kit (DNA Technologies, Inc., Rockville, MD) following the manufacturer's instructions. Densitometry will be used to measure the relative quantity of mRNA (of the putative differentially expressed gene being investigated) present in the samples (calculated as the differentially expressed gene:18S ratio).

**Progress:** Protocol has been amended to include samples gathered at the University of Tennessee, Memphis. Investigators are currently awaiting for IRB approval from that institution prior to collection of more samples and completion of the study.

### Detail Summary Sheet

|                        |                        |                        |
|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/146 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Biomedical Research or Training Using Animal Tissues Only

**Principal Investigator:** CPT Craig Koeller, VC

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** None.

**Keywords:** biomedical research, training labs, animal tissues

**Start Date:**  
9/13/2000

**Est. Completion Date:**  
Sep 03

**Periodic Review:**  
12/5/2001

**Study Objective:** To reduce live animal use in biomedical research or training at MAMC, by facilitating animal tissue use as alternative research/training models, where feasible.

**Technical Approach:** Animal cadavers or tissues used under this protocol will be derived from MAMC IACUC-approved animal use protocols, other AAALAC accredited research institutions, or from local commercial slaughter houses unless otherwise specified in addenda and approved by the IACUC in advance of procurement. This document will serve as a generic, IACUC-approved protocol providing specifications and assurances for animal tissue use in biomedical research or training, which will be adhered to by all persons using this protocol. Specific activities differing from the generic provisions of this protocol will require description and/or justification by addendum, and IACUC approval, prior to conducting the described research or training.

**Progress:** This addendum specific protocol was amended during FY02 to allow for animals previously sacrificed on other IACUC approved protocols to be used for bench research. All animal use resulting from this protocol has been reported in the protocol where the animal was originally used. This protocol remains ongoing under the direction of the new DCI veterinarian.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/073                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Comparative Medical/Surgical Research and Development (Limited) |  |                                      |
| <b>Principal Investigator:</b> CPT Craig Koeller, VC                          |  |                                      |
| <b>Department:</b> Clinical Investigation                                     |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> None.                                       |  |                                      |
| <b>Keywords:</b> animal study, training                                       |  |                                      |
| <b>Start Date:</b><br>3/8/2000  | <b>Est. Completion Date:</b><br>Mar 03 | <b>Periodic Review:</b><br>6/20/2001 |

**Study Objective:** (1) To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients; in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC and (2) To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies, and surgical advancement training proposed by MAMC-affiliated medical staff.

**Technical Approach:** This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) development or refinement of animal models for medical/surgical research or training; b) limited pilot studies (animal) that are preliminary to more extensive research proposals; c) practice of newly described surgical procedures, in animal models, prior to utilization in the MAMC human surgical patient population. Animal use in these investigative pursuits will generally be limited to not more than four (4) animals per co-investigator or procedure, and will be conducted as acute (non-survival) experiments unless animal survival is specifically justified. Details of proposed model development or refinement, pilot studies, or surgical procedure practice will be provided as procedure specific addenda to this standing protocol. This protocol will only be used for preliminary pilot/model development and MAMC surgical care advancement, and will not be used to generate data sufficient for publication in scientific journals.

**Progress:** This protocol was not utilized during FY 02. The study remains ongoing for pilot animal model protocols.

### Detail Summary Sheet

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|                        |                       |                        |
|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 95/025 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** The Department of Clinical Investigation's Molecular Biology Short Course for Physicians

**Principal Investigator:** CPT Patrick M. McNutt, MS

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**Department:** Clinical Investigation

**Facility:** MAMC

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**Associate Investigator(s):** CPT Todd M. Rossignol, MS; MAJ Rodger K. Martin, MS; CPT Wade K. Aldous, MS; CPT Aziz N. Qabar, MS

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**Keywords:** Molecular biology, training course

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|                    |                              |                         |
|--------------------|------------------------------|-------------------------|
| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
|--------------------|------------------------------|-------------------------|

1/20/1995

Jun 96

12/10/2001

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**Study Objective:** To familiarize MAMC residents, fellows, and staff physicians with the research capabilities and resources of the Department of Clinical Investigation. To support MAMC Graduate Medical Education through instruction and research. To foster an appreciation of molecular biology concepts in residents, fellows, and staff physicians and to augment their understanding of the scientific literature. To encourage residents, fellows and staff physicians to develop research protocols incorporating these technologies.

**Technical Approach:** This course is designed to familiarize physicians with the most commonly encountered molecular approaches in the scientific and clinical literature. It is hoped that this will foster more critical reading of the literature as well as encouraging the development of research protocols employing these technologies. Although six weeks in duration, students will be required to attend two hours of lecture per week in addition to approximately seven hours of laboratory exercises. Topics addressed and used in the course range from DNA isolation to cloning and sequencing of PCR products.

**Progress:** The molecular biology short course was not given during FY02. The new principal investigator, CPT Patrick McNutt, MS, plans to present the short course during the first months of 2003.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 201/032

**Status:** Ongoing

**Title:** Birth Weight as a Function of Maternal Duty Status and Participation in Mandatory Physical Training Program

**Principal Investigator:** Troy H. Patience, B.S.

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** COL Robert E. Ricks, MC; COL Byron C. Calhoun, MC, USAF; CPT Melissa V. Terry, MC; LCDR Mary G. Battaglia, NC, USNR; COL Roderick F. Hume, MC; MAJ Katherine M. Opitz, AN; CPT Sandra L. Hernandez, MC; CPT Kim Whittington, MC

**Keywords:** Birth weight, PSWP, maternal duty status, maternal exercise, military specific

**Start Date:**  
1/23/2001

**Est. Completion Date:**  
Oct 02

**Periodic Review:**  
11/27/2001

**Study Objective:** Conflicting reports have confused the impact of maternal work or physical activity upon fetal development. The majority of pregnant women work outside the home. Active duty soldiers are a special case of workers. One of the requirements to remain on active duty is maintaining physical fitness standards for gender and age group. Specifically designed exercise programs for pregnant and postpartum soldiers have been ongoing at Ft. Lewis for several years. Voluntary and mandatory participation depends upon active duty unit assignment. All active duty pregnancies are cared for by the OB department at MAMC, MFM/DCI consults for the PSWP, the vast majority of participants deliver at MAMC. Therefore, we propose to tabulate birthweights and percentile for gestational age at delivery to compare those newborns of active duty who did or did not participate in the PSWP, and matched dependent wives as controls.

**Technical Approach:** Does maternal work or working out alter birth weight. Existing medical records (CHCS, CIS and Birth Register) will be reviewed to collect pertinent information in coded files (no linkage to person). Current duty status (20- vs 30), maternal age, gestational age at delivery, birth weight and complications are in the Delivery Books. CHCS & CIS maintain the obstetrical records; which will be reviewed by AI (MT, EH) to verify smoking, maternal ponderal index and diabetes status. PSWP participant duty roster is maintained as an EXCEL data sheet. Correlations for each case (AD-+PSWP & AD- not PSWP) will be matched to the next same age, parity and gestational age birth in the record. Data collection will be by the AI (RFH) on a Filemaker Data record designed for this purpose by the PI. Three cumulative distribution curves of birth weight by gestational age will be generated for 20+, 20-, & 30. Confounders include smoking status, parity, race, and gestational diabetes. Maternal ponderal index will be calculated from height and weight; neonatal percentile will be calculated from birth weight by gestational age at birth reported as a percentile and categorized as LGA (>90<sup>th</sup> percentile), AGA or SGA (<10<sup>th</sup> percentile). Major question is does maternal duty status, or mandatory exercise lead to smaller babies, or more preterm or SGA births?

**Progress:** Retrospective review, no study enrollment. Entering data from hardcopy records. Still in data entry phase. No analysis during FY02.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/006      **Status:** Completed

**Title:** Effect of JP-8 Fuel and Fuel Exhaust on Markers of Inflammation and Immune Function in Exposed Workers Compared to a Non-exposed Cohort

**Principal Investigator:** CPT Todd M. Rossignol, MS

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** Terri L. Blake, Ph.D.; MAJ Thomas C. Delk, MS; Greg S. Opheim, RPIH; David N. Weissman, M.D.; Mr. Mark A. Lucas, MS; James R. Wright, BA, MT (ASCP); Mr. Louis A. Matej, B.S.; Mr. Ernest R. Crutcher, IH; CPT Shannon N. Shaw, MS; CPT Derek J. Licina, MS; Mr. Lynn B. Whittern, IH

**Keywords:** mixed exposures, JP-8, nasal lavage, inflammation, immunity

**Start Date:**  
10/24/2000

**Est. Completion Date:**  
Aug 01

**Periodic Review:**  
10/23/2001

**Study Objective:** 1) Analyze nasal lavage and blood samples from JP-8 exposed and non-exposed workers for markers of inflammation and immune function. 2) Collect cells by nasal scraping from these workers for analysis of induction of transcription of specific genes: CYP1A1, AhR, and AhR-NT. 3) Administer a questionnaire focused on pulmonary function and illness in these workers. 4) Collect personal and ambient air samples for analysis.

**Technical Approach:** This study is a NIOSH funded collaboration with the DOD to describe the exposure of a cohort of Ft. Lewis workers exposed to engine exhaust compared to a cohort of workers not routinely exposed to exhaust. 60 workers in each cohort (120 total) will undergo nasal swabbing to collect cells and nasal lavage for assessment of cytokine levels by ELISA (IL-1, IL-6, IL-8, TNF-alpha, and MIP-1). A 5 ml blood sample will be used to measure serum IG-E. These biomarkers will be used to assess the degree of upper respiratory inflammation and immune response. Personal and worksite area air sampling will also be performed to describe the composition of the fuel exhaust. Members of each cohort will answer a standardized questionnaire about work and smoking history and respiratory symptoms. Study results will be reported to NIOSH and published in peer-reviewed journals in order to direct future research into potential health effects of engine exhaust exposure.

**Progress:** All data collection for this study has been completed, effective 10 Jul 02. An abstract of the findings is not yet available.



### Detail Summary Sheet

|  |  |                                       |
|--|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/043                 | <b>Status:</b> Terminated             |
| <b>Title:</b> Immunohistochemical and Molecular Biotechnologic Detection of the Human Adrenomedullin Receptor  |  |                                       |
| <b>Principal Investigator:</b> CPT Todd M. Rossignol, MS   |  |                                       |
| <b>Department:</b> Clinical Investigation  | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> COL Roderick F. Hume, MC; MAJ Christina C Apodaca, MC; COL Byron C. Calhoun, MC, USAF; James R. Wright, BA, MT (ASCP); Mr. Louis A. Matej, B.S.  |  |                                       |
| <b>Keywords:</b> adrenomedullin, adrenomedullin receptor, human placenta, immunohistochemistry, western blot analysis, polyclonal antibody   |  |                                       |
| <b>Start Date:</b><br>2/22/2000  | <b>Est. Completion Date:</b><br>Sep 00 | <b>Periodic Review:</b><br>12/10/2001 |
| <b>Study Objective:</b> (1) Produce a polyclonal antibody that recognizes both the native and denatured forms of the human adrenomedullin receptor. This will allow the detection of this receptor in both immunohistochemical assays and western blot analysis. (2) Perform immunohistochemical assays and western blot analysis on various compartments of the human placenta.   |  |                                       |
| <b>Technical Approach:</b> A peptide sequence corresponding to amino acids 5-19 and 244-254 of the human adrenomedullin receptor will be sent to Sigma Genosys to be synthesized and conjugated to KLH. This peptide will then be used to produce polyclonal antibodies. Once the antibodies are produced, preliminary immunohistochemical assays will be run to determine the proper dilution of the antibody. In order to verify that the antibody is recognizing the intended protein, the antibody is pre-incubated with the purified antigen. Upon identifying eligible placentas, the primary investigator will be notified at the time of the delivery. The placenta will be obtained immediately after delivery and placed on ice. Approximately 5 grams each of the placental amnion, cotyledon, umbilical vein and umbilical artery will be dissected and isolated. 1-2 cm2 area of the frozen tissues sections will be mounted on the cryostat using OCT. The tissues will be sliced into 5-10 uM sections. These sections will be probed with the primary antibody (Rabbit Anti-Adrenomedullin Receptor IgG) after being blocked and then after washing they will be probed with the secondary antibody (Mouse Antirabbit IgG) conjugated with Fluorescein Isothiocyanate (FITC). The slides will be viewed using a fluorescent microscope with an excitation wavelength of 450-490 nm and filtered at 520-560 nm. |  |                                       |
| <b>Progress:</b> Protocol terminated due to its cost and validity of study design.   |  |                                       |

### Detail Summary Sheet

|                        |                        |                           |
|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/130 | <b>Status:</b> Terminated |
|------------------------|------------------------|---------------------------|

**Title:** Production of Anti-Adrenomedullin Receptor Monoclonal Antibodies in Mus musculus

**Principal Investigator:** CPT Todd M. Rossignol, MS

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** Mr. Louis A. Matej, B.S.; James R. Wright, BA, MT (ASCP); COL Byron C. Calhoun, MC, USAF; COL Roderick F. Hume, MC

**Keywords:** mouse adrenomedullin monoclonal antibody receptor

**Start Date:**  
7/11/2001

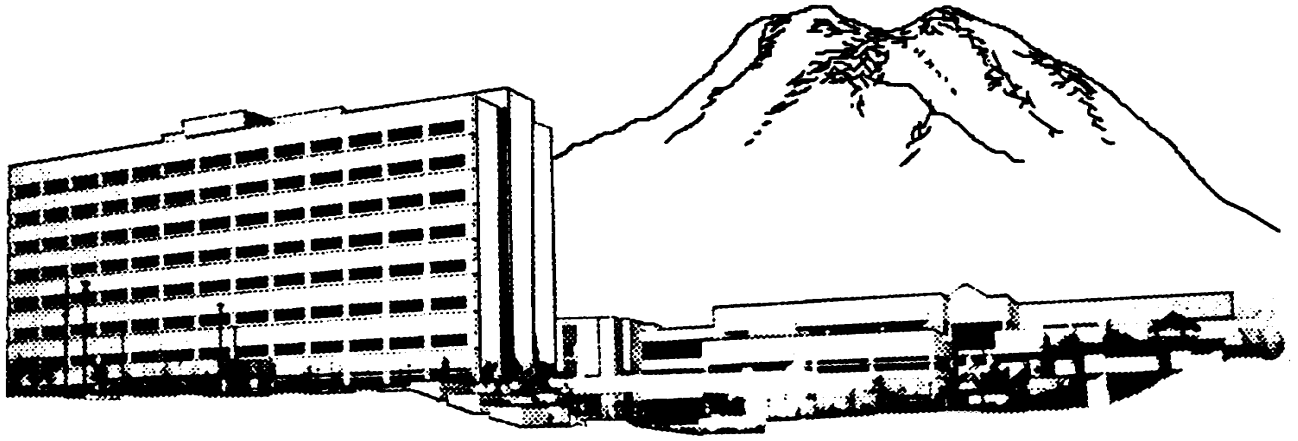
**Est. Completion Date:**  
Jul 04

**Periodic Review:**

**Study Objective:** To produce a monoclonal antibody that is specific for the human adrenomedullin receptor in order to evaluate the following hypothesis: Preeclamptic human placental tissues express a lower level of the adrenomedullin receptor than do normal placentas.

**Technical Approach:** This protocol proposes the use of not more than 10, Balb/c mice to produce adrenomedullin receptor protein-sensitized hybridoma cells by injecting purified adrenomedullin antigen into mouse spleens, stimulating non-differentiated B-lymphocytes to replicate and differentiate into anti-adrenomedullin plasmocytes (AAP). Mice will be euthanized four (4) days after spleen injection, and AAPs will be separated from splenic homogenate and fused to commercially available mouse myeloma cells to form anti-adrenomedullin hybridoma cells (AAH). Anti-adrenomedullin hybridoma cells will then be cultured to produce monoclonal anti-adrenomedullin antibody for immunohistochemical detection of adrenomedullin in normal and preeclamptic human placenta tissues.

**Progress:** This protocol was terminated, as the study methods relied on results from another protocol which was ultimately terminated. No work was done on this protocol.



## **Detail Summary Sheets**

### **Hospital Dental Clinic**

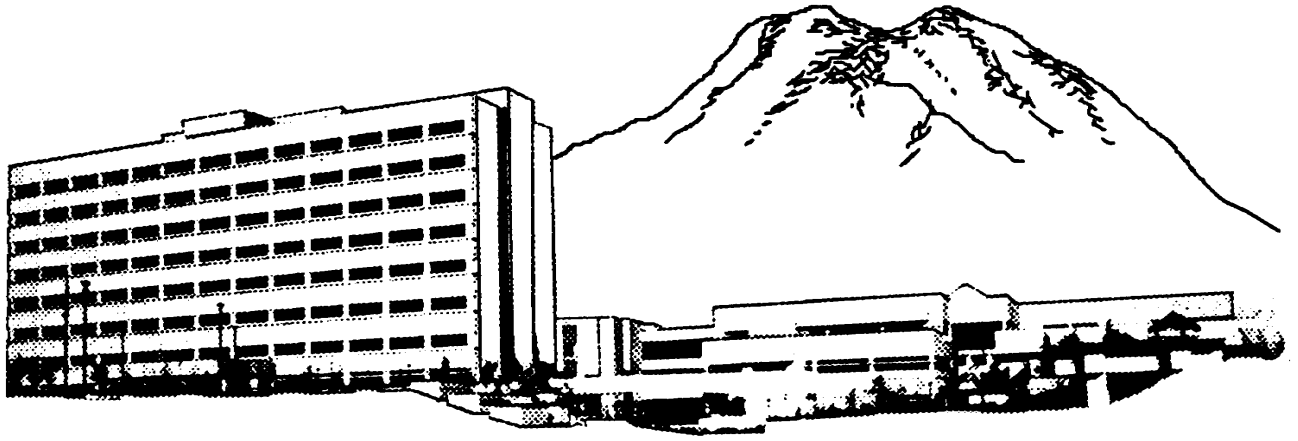
### Detail Summary Sheet

|  |  |  |                        |
|--|--|--|------------------------|
| <b>Date:</b> 30 Sep 02   |  | <b>Number:</b> 202/068                 | <b>Status:</b> Ongoing |
| <b>Title:</b> Septotomy with a Surgically Assisted Maxillary Expansion |  |  |                        |
| <b>Principal Investigator:</b> CPT R. Eric Bessey, DC                  |  |  |                        |
| <b>Department:</b> Dentistry   |  | <b>Facility:</b> MAMC                  |                        |
| <b>Associate Investigator(s):</b> ; MAJ David R. Beanland, DC          |  |  |                        |
| <b>Keywords:</b> Septotomy, Surgically Assisted Maxillary Expansion    |  |  |                        |
| <b>Start Date:</b><br>5/28/2002  |  | <b>Est. Completion Date:</b><br>May 03 |                        |
|  |  | <b>Periodic Review:</b>                |                        |

**Study Objective:** Many patients have facial skeletal deformities requiring surgical correction. Maxillary hypoplasia (midface deficiency) is a common surgical referral. These patients have a small upper jaw and severe dental crowding. It requires a Lefort Osteotomy or a Subtotal Lefort Osteotomy (Surgically Assisted Maxillary Expansion-SAME) to expand and/or reposition the maxillary. We are proposing a prospective, double-blind, randomly controlled study to compare two different surgical techniques to expand the upper jaw. The basic approach is using a series of bony cuts to the supporting bones (butteresses) of the face. The SAME procedure requires an osteotomy through the nasal piriform rim, lateral nasal walls, zygomaticomaxillary buttress, posterior maxilla, and separation of the maxilla from the pterygoid plates.

**Technical Approach:** Referred patients from an Orthodontist with a history of transverse maxillary hypoplasia and severe maxillary dental crowding will be evaluated for surgical acceptance to receive a surgically assisted maxillary expansion. Thirty (30) patients will be randomized into two groups, a control group and a group that will receive septotomy as part of the surgical procedure. Pre-surgical computerized tomography will be done to measure the intra-nasal space. Each group will undergo a surgically assisted maxillary expansion in the Main Operating Room of Madigan Army Medical Center. Blood loss will be measured at completion of the surgery, as well as length of procedure. A transpalatal expansion device will be activated intra-operatively in the usual fashion. Patient will self adjust this TPE as directed by the Orthodontist until necessary maxillary expansion is achieved. Post operatively the patient will be seen, per our usual protocol, on a weekly basis for followup and questioning of post-operative complications. After the completed movement a post-operative CT scan will be taken with the patients head placed in the same position as the preoperative scan. The same points will be measured to evaluate any significant difference between the two surgical techniques. An unpaired t-test will be used to compare the movements of the septum, blood loss, length of surgery and post operative morbidity between the two groups.

**Progress:** Three patients have been enrolled during FY02. One patient has had the surgery. Two are scheduled for the near future. CT scans were successfully taken on all three with the aid of Radiology. The first patient is currently in the movement phase of the study. There have been no unexpected events with the protocol.



## **Detail Summary Sheets**

### **Department of Emergency Medicine**

### Detail Summary Sheet

|  |  |                                      |
|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/070                  | <b>Status:</b> Terminated            |
| <b>Title:</b> A Survey to Determine the Incidence of Infection in Plantar Puncture Wounds    |  |                                      |
| <b>Principal Investigator:</b> CPT Charles P. Buck, MC                                       |  |                                      |
| <b>Department:</b> Emergency Medicine  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> CPT Austin W. Burgess, MC; LTC David A. Della-Giustina, MC |  |                                      |
| <b>Keywords:</b> Plantar wound , infection, immune compromised                               |  |                                      |
| <b>Start Date:</b><br>6/22/1999  | <b>Est. Completion Date:</b><br>Jul 99 | <b>Periodic Review:</b><br>6/26/2001 |

**Study Objective:** To determine the incidence of infection in plantar puncture wounds, and to determine if infection rates are different for healthy vs. immune compromised and aggressive vs. conservative initial management groups.

**Technical Approach:** All adult ambulatory patients identified by the triage nurse as having a prior plantar puncture wound will be asked to complete an anonymous survey. Investigators will periodically collect the forms and transfer the data to spreadsheets for further analysis. Method of data analysis: Primary is the overall incidence of infection of plantar puncture wounds, with data analyzed at 95% confidence intervals. Secondary is the infection rate for two groups, which will consist of subjects that had aggressive initial treatment vs. conservative treatment, and those who were healthy at the time of injury vs. those with vascular or immuno-compromising diseases. These groups will be analyzed by Chi-Square to determine statistical significance at  $p < 0.05$ .

**Progress:** Due to the PCS of the principal investigator, and no new investigator assigned, this study has been terminated at MAMC.

### Detail Summary Sheet

|   |  |                          |
|---|--|--------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/135                 | <b>Status:</b> Completed |
| <b>Title:</b> Oral Dexamethasone in the Emergency Department to Prevent Relapse of Acute Migraine Headaches: A Randomized, Placebo Controlled Trial                               |  |                          |
| <b>Principal Investigator:</b> CPT Michael C. Hirsig, MC  |  |                          |
| <b>Department:</b> Emergency Medicine   |  | <b>Facility:</b> MAMC    |
| <b>Associate Investigator(s):</b> MAJ David A. Siegel, MC; CPT Brian Ness, MC; CPT Tim Gregory, MC; CPT Brad A. Kilcline, MC; CPT Timothy S. Talbot, MC; CPT Jeremiah Johnson, MC |  |                          |
| <b>Keywords:</b> dexamethasone, migraine, headache, abortive therapy, emergency   |  |                          |
| <b>Start Date:</b><br>9/25/2001   | <b>Est. Completion Date:</b><br>Feb 02 | <b>Periodic Review:</b>  |

**Study Objective:** To determine the incidence of recurrence of migraine headaches up to 24 hours after discharge from the emergency department and to determine if oral dexamethasone given in the emergency department will lead to a reduction in patient revisits for headache at 24 hours.

**Technical Approach:** This study plans to enroll 120 and will include males and females aged 18-65 with known history of migraine headache presenting to the ED with a chief complaint of headache. During initial evaluation patients will be informed of the study and asked to consent. Their migraine will be treated according to study protocol if patient consents. The physician will fill out a questionnaire that asks the patient to rate their headache at presentation and discharge (visual analog scale of 0-10, 0 being no headache, 10 being worst headache of life). Patients will then be asked to take the study drug (which will be randomized in plastic bags). The patient is then discharged from the ED and told they will be contacted in 1-2 days and asked if they had to seek additional medical care for their headache or if they had to use any rescue medications that were prescribed to them in the past 24-48 hours. Patients will also receive a self-addressed stamped envelope with a visual analog scale attached and asked to mail the completed scale back to the investigators. Once the final number is reached, the code of the randomized numbers will be revealed and the data will be tabulated regarding the control group's demographic, pain scale data vs. the treatment groups demographic and pain scale data. Outcome variables are headache at 24-48 hours causing the patient to seek additional medical care and a secondary outcome of use of rescue medication.

**Progress:** 37 patients enrolled in this study over the last 12 months with no adverse reactions noted. However, the study had to be stopped when IV compazine became unavailable. A summary of the data analysis is pending.

### Detail Summary Sheet

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|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/080 | <b>Status:</b> Terminated |
|------------------------|------------------------|---------------------------|

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**Title:** Impact of Chest Radiography Results on Clinician Decision-making for Young Adult Patients Presenting to the Emergency Department with Non-traumatic Anterior Chest Pain, Normal Vital Signs and a Normal Physical Exam

**Principal Investigator:** CPT Nicholas Martyak, MC

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**Department:** Emergency Medicine

**Facility:** MAMC

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**Associate Investigator(s):** Marcus A. Trione, M.D.; LTC David A. Della-Giustina, MC; CPT Walter A. Fink, Jr., MC; MAJ Robert K. Lather, MC

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**Keywords:** physician decision-making, chest pain, x-ray, radiograph, emergency department, outpatient

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**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
6/26/2001

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**Study Objective:** The purpose of this study is to evaluate the impact of chest radiography on clinical decision-making in young adult patients presenting to an Emergency Department with non-traumatic anterior chest pain, normal vital signs and a normal physical exam.

**Technical Approach:** This study will be a prospective evaluation of clinical decision making by ED physicians. Physicians will be asked to present a pretest diagnosis and treatment plan with disposition prior to interpreting the chest radiograph. Diagnosis and treatment plan will then be assessed in light of the chest radiograph. Finally, the physician will be asked to assess whether the chest radiograph altered the patient's diagnosis or treatment plan. For both diagnosis and treatment, the physician will be asked to classify the change from pre- to post-interpretation as incidental or major. This study's goal is to assist in the generation of rational, evidence-based guidelines for the use of chest radiography in this low-risk (military) population.

**Progress:** No patients enrolled during FY02. The initial investigators have left and further recruitment has been severely impaired. As such, the protocol has been terminated.



### Detail Summary Sheet

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|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 97/020                  | <b>Status:</b> Ongoing                |
| <b>Title:</b> A Model for Prehospital 12-Lead Acquisition Without A Dedicated 12-Lead ECG Machine |  |                                       |
| <b>Principal Investigator:</b> Steven A. Pace, MD   |  |                                       |
| <b>Department:</b> Emergency Medicine   |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> Fritz P. Fuller, N.R.E.M.T.-P; COL Alice M. Mascette, MC        |  |                                       |
| <b>Keywords:</b> ECG:12 lead  |  |                                       |
| <b>Start Date:</b><br>2/21/1997   | <b>Est. Completion Date:</b><br>May 96 | <b>Periodic Review:</b><br>12/18/2001 |

**Study Objective:** To verify that a 12-lead ECG obtained with a cardiac monitor/defibrillation unit is comparable in accuracy to that of a dedicated 12-lead ECG machine.

**Technical Approach:** The management of ischemic chest pain and acute myocardial infarction hinges on early diagnosis and treatment with thrombolytic agents if indicated. It has been shown that prehospital recognition of acute MI using 12-lead electrocardiography and interpreted by nurses/paramedics trained in ECG evaluation can result in significantly faster times to thrombolytics compared to patients who did not receive a prehospital ECG. Today there are several portable 12-lead machines with computer assisted diagnosis available, but they have only recently become available and are very expensive. By utilizing a portable 12-lead machine (Lifepak 10) and demonstrating that it can produce diagnostic quality ECG's, we hope to make available to a large group of prehospital providers 12-lead capability without an increased monetary investment.

**Progress:** No new data collection occurred during FY02. Analysis of data is ongoing. No conclusions have been drawn yet.

### Detail Summary Sheet

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|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/007 | <b>Status:</b> Terminated |
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**Title:** Is There Any Additional Efficacy in Adding Single Dose Intravenous Antibiotic Therapy to an Oral Antibiotic Regimen for Uncomplicated Cellulitis?

**Principal Investigator:** MAJ David A. Siegel, MC

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|---------------------------------------|-----------------------|
| <b>Department:</b> Emergency Medicine | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT Thomas R. Coomes, MC; MAJ Danny O. Stene, MC; CPT John Westhoff, MC; Janet H. Shotwell, M.D.; MAJ Robert W. Desverreaux, MC

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**Keywords:** cellulitis, cephalosporin, parenteral antibiotic

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**Start Date:**

10/26/1999

**Est. Completion Date:**

Nov 02

**Periodic Review:**

2/21/2002

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**Study Objective:** To determine if there is any additional efficacy in adding single dose intravenous antibiotic therapy to an oral antibiotic regimen for uncomplicated cellulitis.

**Technical Approach:** Subjects with cellulitis will be enrolled and randomly assigned into one of two treatment arms. The first arm will receive intravenous cefazolin, and the second arm will receive a parenteral placebo. All subjects will receive a 10-day course of oral cephalexin. Clinical indicators will be assessed and compared at days 7 and 14.

**Progress:** The principal investigator requested this study be terminated, 26 Feb 02, due to poor enrollment.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/103                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Clinical Utility and Performance of the Intubating Laryngeal Mask Airway in the Special Operations Environment |  |                         |
| <b>Principal Investigator:</b> CPT Timothy S. Talbot, MC   |  |                         |
| <b>Department:</b> Emergency Medicine  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> LTC Ian S. Wedmore, MC; CPT Peter J. Cuenca, MC; CPT Paul Ryan, MC; CPT David Nieman, SP   |  |                         |
| <b>Keywords:</b> Airway, ILMA, Special Operations, Simple Airway, Difficult Airway, Manikin                                  |  |                         |
| <b>Start Date:</b><br>8/27/2002  | <b>Est. Completion Date:</b><br>Apr 02 | <b>Periodic Review:</b> |

**Study Objective:** To determine if a successful airway can be obtained with the ILMA in a Intubating Manikin under operational circumstances

**Technical Approach:** 1. Cohort will perform standard ILMA insertion on an Intubating Manikin as a part of regularly scheduled biannual airway training. Initial attempt will occur with only the LMA information insert available. Subjects will be evaluated by the investigators in an isolated room. No information regarding outcomes will be provided other subjects or unit cadre. All subjects will be assigned a number with no linking of data to name, ssn, or rank. Each will receive two attempts to place the ILMA within 60 seconds for each attempt. 2. Placement attempts will be catalogued as GO/NOGO and percentages will be tabulated. 3. Cohort will receive ILMA training. 4. ILMA insertion will be performed on the manikin. Each will get 2 attempts to place the ILMA within 60 seconds for each attempt

**Progress:** A total of 24 special operations medics (EMT-B) were enrolled. EMT-B trained medics were able to successfully ventilate and intubate using the ILMA prior to training and with increasing frequency with 1/2 hr training. This doubled the previously published successful intubation rates among EMT-B previously published in EM literature. Data is being tabulated for pending publication in Emergency Medicine Literature

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/116 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Intravenous Atropine versus Intravenous Lorazepam for the Treatment of Peripheral Vertigo

**Principal Investigator:** CPT Timothy S. Talbot, MC

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**Department:** Emergency Medicine

**Facility:** MAMC

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**Associate Investigator(s):** LTC Ian S. Wedmore, MC; CPT Marc E Levsky, MC; Gregory P. Garcia, M.D.

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**Keywords:** atropine lorazepam peripheral vertigo emergency department sedation

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**Start Date:**

9/24/2002

**Est. Completion Date:**

Jul 03

**Periodic Review:**

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**Study Objective:** To determine if IV Atropine is as effective as IV Lorazepam in the treatment of peripheral vertigo in the emergency room setting

**Technical Approach:** This randomized blinded prospective trial seeks to determine if atropine is as effective as lorazepam in relieving the symptoms of peripheral vertigo as well as being treated with less impact from the sedating effects of benzodiazepines. The patient will be screened against inclusionary and exclusionary criteria and enrolled if appropriate. Each patient will receive the study drug, which will be blinded to the treating physician. Thirty minutes after treatment the patient will be assessed by the treating physician on ability to ambulate, ability to be discharged to home as well as assessment of sedation using the NAS Scale. Patient will be discharged home with written directions on how to perform a modified Epley maneuver and will be expected to complete this at a minimum three times over the next 24 hours. An investigator will contact the patient within 48 hours to assess return of symptoms, use of other medications, or other treatment sought.

**Progress:** Study was recently approved. Enrollment to begin soon.

### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/093                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Intubating Laryngeal Mask Airway versus Laryngoscopy and Endotracheal Intubation in the NBC (Nuclear, Biological, and Chemical) Environment   |  |                         |
| <b>Principal Investigator:</b> CPT Timothy S. Talbot, MC  |  |                         |
| <b>Department:</b> Emergency Medicine   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> LTC Ian S. Wedmore, MC; CPT Peter J. Cuenca, MC   |  |                         |
| <b>Keywords:</b> Intubation, Intubating LMA, NBC, Protective Mask   |  |                         |
| <b>Start Date:</b><br>7/23/2002   | <b>Est. Completion Date:</b><br>Jun 02 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> To determine if successful intubation can be obtained with the Intubating LMA versus standard Endotracheal Intubation in an Intubating Manikin in a simulated NBC environment   |  |                         |
| <b>Technical Approach:</b> 1. Cohort will perform standard endotracheal intubation under Protective Mask conditions. Each will get 2 attempts to intubate within 90 seconds2. Intubation attempts will be catalogued as GO/NOGO and percentages will be tabulated3. Cohort will be conduct ILMA insertion untrained except for 10 minutes of reading the ILMA handout. Two attempts will be allowed within 90 seconds. 4. The group will then receive the standard training video and will attempt intubation using the ILMA. Again they will have 2 attempts to intubate within 90 seconds |  |                         |
| <b>Progress:</b> A total of 15 EM residents and staff were enrolled in the study. Results obtained showed that intubation with the M-40 mask using standard techniques were successful on 78% of techniques and intubation using the Intubating LMA was 100% successful. Data is currently pending publication in Military Medicine.  |  |                         |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/099 | <b>Status:</b> Ongoing |
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**Title:** Cosyntropin Versus Caffeine for the Treatment of Post-Dural Puncture Headaches

**Principal Investigator:** CPT Bradley N. Younggren, MC

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**Department:** Emergency Medicine

**Facility:** MAMC

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**Associate Investigator(s):** CPT Wesley G. Zeger, MC; MAJ Kurtis R. Holt, MC

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**Keywords:** post-dural puncture headaches, ACTH, cosyntropin, treatment: headache, caffeine

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**Start Date:**

7/23/2002

**Est. Completion Date:**

Mar 03

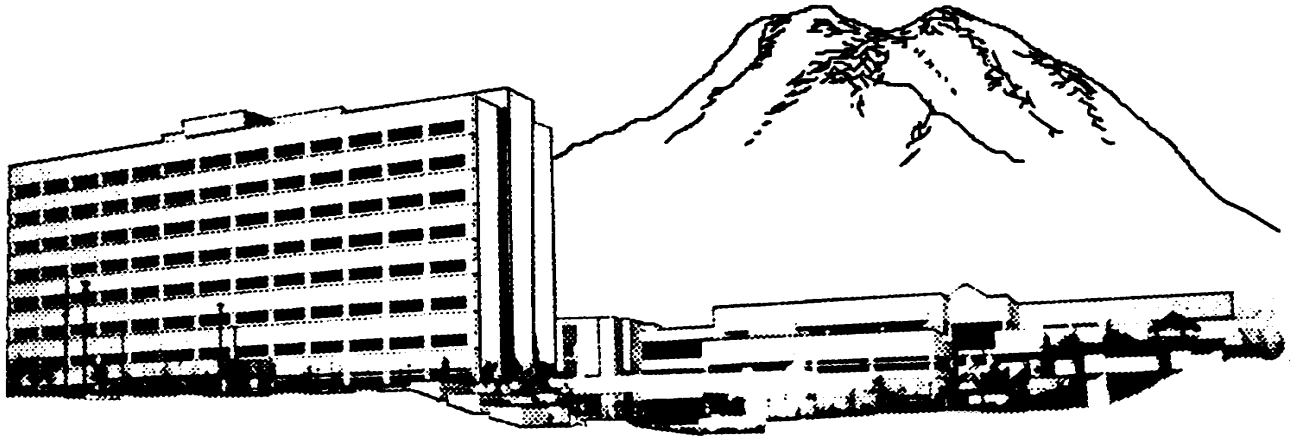
**Periodic Review:**

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**Study Objective:** To investigate the utility of the ACTH analog, Cosyntropin, in patients who present to the emergency department with post dural puncture headaches.

**Technical Approach:** We propose a double-blinded, randomized trial of cosyntropin versus caffeine for post-dural puncture headaches. Eligible patients who elect to enroll in the study will be 18 years of age or older and diagnosed with post-dural puncture headache. Patients will be randomized to receive 0.75 mg cosyntropin IV in 1L NS over 1 hour followed by 1 L NS over one hour, or will be given 1 gram caffeine IV given in 2 sequential 500 mg doses over 2 hours. At 2 hours, rescue therapy will be offered if patients receive inadequate pain relief. Frequency of rescue therapy will be the primary endpoint which will be analyzed with a Chi squared or Fisher's exact test.

**Progress:** This study recently received IRB approval and has not yet been initiated at MAMC.



## **Detail Summary Sheets**

### **Department of Family Practice**

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/042 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

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**Title:** Identifying Relevant Barriers to Breastfeeding in Active Duty Soldiers Using a Theory of Planned Behavior-based Model

**Principal Investigator:** CPT Hillary Arnold-Hurtado, DO

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**Department:** Family Practice

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Mary V. Krueger, MC; CPT Jennifer N. Reynard, MC; COL Thomas C. Michels, MC

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**Keywords:** Breastfeeding, employment, military, weaning, retention, and theory of planned behavior, military specific

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**Start Date:**  
2/27/2001

**Est. Completion Date:**  
Mar 02

**Periodic Review:**

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**Study Objective:** (1) To use the theory of planned behavior-based structural model for breastfeeding to determine what factors prevent active duty military females from initiating breast feeding, (2) To use the theory of planned behavior-base structural model for breastfeeding to determine what factors cause active duty military females to stop breastfeeding prematurely, (3) To evaluate active duty women's rates of breastfeeding intention prenatally, initiation at birth and continuation at eight weeks postpartum and compare them to the rates of their employed civilian peers and (4) To determine active duty military female's prenatal and postpartum attitudes towards and knowledge about breastfeeding.

**Technical Approach:** Names of prospective subjects will be obtained from a list of patients participating in the Pregnant Soldier Wellness program. This is a program in which all I Corps pregnant soldiers must participate. After giving consent for participation, subjects will complete a survey of infant feeding attitudes at the time of a regularly scheduled OB visit. Survey items will include demographic information as well as questions about work environment and attitudes (reverent beliefs), attitudes toward breast and formula feeding (behavioral beliefs), breastfeeding knowledge, perception of control (control beliefs) and intent of infant feeding type. At time of delivery, method of feeding will be recorded in the patients' electronic record. This data will be used to determine breastfeeding initiation rate. At eight weeks postpartum, a second survey will be conducted. This will address the actual barriers that were encountered by the patient, as well as the perceived insufficient milk factor. Information on method of infant feeding will also be obtained.

**Progress:** Dr. Mary Krueger submitted the final conclusions from the study as her masters thesis at University of Washington. In addition she has presented the data in poster form at various national meetings. Details are available in DCI.



### Detail Summary Sheet

|   |  |                                     |
|---|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/107                 | <b>Status:</b> Terminated           |
| <b>Title:</b> Prevention of Unintended Pregnancy in the Military: A Multicenter Randomized Clinical Trial   |  |                                     |
| <b>Principal Investigator:</b> LTC Diane M. Flynn, MC   |  |                                     |
| <b>Department:</b> Family Practice  |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> ; COL Jeffrey D. Gunzenhauser, MC; COL Roderick F. Hume, MC; Ann K. Lancaster, CHN; MAJ Wanda A. Barfield, MC; MAJ Sherri Baker, AN |  |                                     |
| <b>Keywords:</b> unintended pregnancy,, state of change, military specific  |  |                                     |
| <b>Start Date:</b><br>6/27/2000   | <b>Est. Completion Date:</b><br>Dec 04 | <b>Periodic Review:</b><br>6/7/2002 |

**Study Objective:** To determine if a 3-hour educational class coupled with a system of facilitated access to health care are an effective strategy to: (1) Decrease the rate of unintended pregnancies among military women ages 18-25, (2) Decrease the rate of unintended paternity among military men ages 18-25, and (3) Advance the stage of behavioral change with respect to contraceptive attitudes among military men and women ages 18-25.

**Technical Approach:** Subjects will be given a questionnaire to determine their attitudes about pregnancy and/or paternity. Subjects will then attend a 3-hour class on reproductive health. After one year, class participants will be again fill out a questionnaire to determine rates of pregnancy/paternity in the previous year and about the outcomes of those pregnancies. Questionnaires will also ask about contraceptive use and behavioral stages of change with regard to contraceptive attitudes.

**Progress:** Due to lack of funding, this protocol has been terminated at MAMC prior to its initiation.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/061 | <b>Status:</b> Ongoing |
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**Title:** Graduate Medical Education and Family Medicine: What Do Young Family Physicians Value Regarding Residency Training Curriculum?

**Principal Investigator:** CPT Mary Lim, MC

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| <b>Department:</b> Family Practice | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LCDR Maureen O. Padden, MC, USN

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**Keywords:** medicine family practice general residency curriculum

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**Start Date:**  
4/23/2002

**Est. Completion Date:**  
Dec 02

**Periodic Review:**

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**Study Objective:** To identify aspects of curriculum in Family Medicine graduate medical education that young Family Physicians value and what changes they believe might benefit the future of Family Medicine.

**Technical Approach:** Participants will be given a 42-item questionnaire asking them to provide demographic information as well as information in regards to their residency training. Responses will then be entered into a master database that contains no identifiers that would link to the subject.

**Progress:** This study remains ongoing for continued data collection.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/039                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Why Do They Go? Investigating Reasons for Attrition of Pregnant Soldiers from the Military |  |                         |
| <b>Principal Investigator:</b> CPT Mary Lim, MC  |  |                         |
| <b>Department:</b> Family Practice   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> MAJ Mary V. Krueger, MC; CPT Elain M. Munitz, MC                       |  |                         |
| <b>Keywords:</b> military pregnancy retention attrition active duty women, military specific             |  |                         |
| <b>Start Date:</b><br>2/26/2002  | <b>Est. Completion Date:</b><br>Sep 02 | <b>Periodic Review:</b> |

**Study Objective:** To identify factors correlated with attrition of pregnant soldiers from military service.

**Technical Approach:** Active Duty pregnant soldiers will be identified at the new obstetrics orientation class or at the Pregnant Soldier Wellness Program and be given a 57 item questionnaire asking them to provide demographic information and their reasons for either terminating their military service or remaining on active duty status. The two main instruments that will be utilized is a 57-question survey that will be distributed to pregnant soldiers at both the new obstetrics class and at the Pregnant Soldier Wellness Program. The first instrument will be directed towards active duty women who have decided to leave the military service during their pregnancy. The second instrument will be distributed to those active duty women who have decided to remain on military service. Each survey is estimated to take approximately 25 minutes to complete. The participants will be asked to place the completed survey in a designated folder/box.

**Progress:** This study remains ongoing to complete its data collection phase.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/073      **Status:** Completed

**Title:** Outcomes of Diabetes Disease Management in a Military Population Using Two Different Models

**Principal Investigator:** LCDR Maureen O. Padden, MC, USN

**Department:** Family Practice

**Facility:** MAMC

**Associate Investigator(s):** LCDR Patrick H. Ginn, MC, USN; CDR John R. Holman, MC; Troy H. Patience, B.S.

**Keywords:** Diabetes Mellitus; Disease Management, military specific

**Start Date:**

4/24/2001

**Est. Completion Date:**

May 02

**Periodic Review:**

3/26/2002

**Study Objective:** The specific aims of this proposal are to identify whether each respective disease management program applied to a cohort of high-risk diabetics will: (1) Improve glycemic control as measured by Hemoglobin A1C (HbA1C), (2) Improve compliance with preventative services, (3) Improve continuity of care with assigned provider, (4) Reduce use of inappropriate portals of access to care (emergency room) and (5) Improve patient satisfaction.

**Technical Approach:** This is a prospective cohort study involving 375 high-risk and 375 low-risk diabetic patients in three separate portals of care being managed by two newly implemented different disease management programs. We will examine emergency room visits and continuity of visits with PCM before and after the intervention.

**Progress:** Diabetes mellitus currently affects 16 million Americans with this number expected to double by 2010. Diabetes accounts for an astounding 15% of health care expenditures, with most costs related to the treatment of preventable complications. The Family Practice Clinic at Madigan Army Medical Center instituted the Diabetes Disease Management Program (DDMP), a two-tiered program aimed at improving the care of diabetes, in May 2001. High-risk patients, with HbA1C values / 8.0%, received a resource intense multidisciplinary approach to care while low-risk patients, whose HbA1C values were £ 7.9% at baseline, received a more basic program. Methods: A retrospective analysis of data collected as part of the DDMP was undertaken to assess program performance. A cohort of 202 patients was evaluated, the primary outcome being improvement in glycemic control as measured by change in mean Hemoglobin A1C values over one year.

Improvement in provision of recommended preventive services, change in mean blood pressure, BMI, lipids and utilization of health care services at the facility were also assessed. Results: The DDMP was effective at improving glycemic control with the effect most pronounced in patients with baseline HbA1C values / 8.0%. There were statistically significant improvements in the provision of recommended preventive services to both cohorts. Utilization of primary care visits increased, as did the percentage of visits where diabetes was addressed. Emergency room visits and inpatient hospitalizations trended downward but without statistical significance. Utilization of endocrinology visits dropped by 50% after program implementation in both cohorts with this change achieving statistical significance in the high-risk cohort and approaching significance in the low-risk cohort. Conclusion: A two-tiered approach to care, utilizing more resources in patients with higher Hemoglobin A1C values, was effective in improving glycemic control and improving the provision of preventive services to all patients, regardless of cohort. Though the highest risk group showed the greatest improvement, patients with HbA1C values < 7.9% also improved while using less resources. The DDMP was successful in improving glycemic control and provision of preventive services in both high-risk and low-risk diabetic patients cared for in a primary care setting.

## Detail Summary Sheet

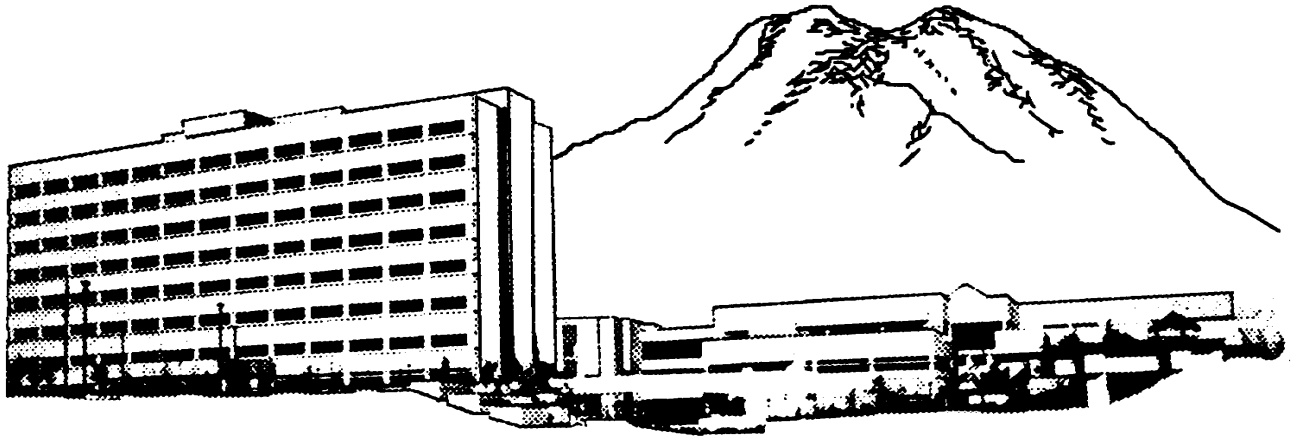
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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/112                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Home Maintenance of Prescriptions and Over-the-Counter Medications: Implications for Morbidity |  |                         |
| <b>Principal Investigator:</b> MAJ David M. Wallace, MC  |  |                         |
| <b>Department:</b> Family Practice   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> COL Allen F. Almquist III, MS;   |  |                         |
| <b>Keywords:</b> Home Maintenance Prescriptions Medications Implications Morbidity                           |  |                         |
| <b>Start Date:</b><br>9/24/2002  | <b>Est. Completion Date:</b><br>Jan 03 | <b>Periodic Review:</b> |

**Study Objective:** Noncompliance, or failure to follow outlined medical therapy, is a health concern that continues to plague the health care system. Evidence suggests that medication prescriptions will increase threefold between the early 1990's and 2010. As the desire for new and more effective drugs increases in America, fewer pharmacists are available to dispense these medications. Preliminary studies suggest that the increase use of medications, combined with a failure to appropriately store or dispose of unused medications, may lead to increased morbidity and health care cost expenditures. Limited data have been collected to analyze the extent of patient hoarding or retaining of non-prescription and prescription medications in their homes. Further research is needed in order to address this hidden health care concern.

**Technical Approach:** The Home Maintenance of Prescription and Over-The-Counter-Medications Study will be initiated by identifying potential enrollees in the descriptive study. All adult patients presenting to the MAMC pharmacy for filling of written prescriptions will be provided with a written questionnaire, containing screening and demographic information. A compilation of potential candidates will be collected over a two to four week period, at which time the survey will be discontinued and an initial study base population will be established. Questionnaires will be reviewed, and those individuals that meet the inclusion (i.e. enrolled in the FPC, adult patients, willing to allow a home visit, etc) and exclusion criteria for enrollment will be assigned a number and selected for the pool of potential home visit patients. Random selection tables will be utilized for determination of the final study population to ensure random selection of patients. Once the study population has been established, patients will be contacted by the PI to arrange for a home visit that is at the convenience of the patient. Home visits will be conducted with the support of not only the primary investigator, but may also include the staff pharmacist of the FPC. Goals for the study are to conduct at least five home visits per week during the period of investigation. On arrival to the patient's home, the visiting staff will introduce themselves with appropriate identification (i.e. military ID card) and restate the purpose of the home visit using a standardized script. Study investigators will leave the home immediately if another adult occupant objects to allowing them in the home. Patients will be advised that the purpose of the home visit is to provide education on proper care, safekeeping and disposal of their prescription, non-prescription, and herbal medications, along with gathering data on some. They will be asked by the investigation team to produce all of the medications that they have maintained in their home. Only medications that are identified by the patient as belonging to, being used by, or prescribed to them will be included in the study. Medications belonging to or prescribed to other family members within the home will be excluded, based on the premise that only the target individual has authorized the home visit and personal review of his or her medications. Data will be collected and documented using pre-established forms, recording patient random ID, medication name, expiration status, and method of obtaining the medication (prescription/non-prescription). Based on the increased use of herbal supplements by individuals, these medications will also be included in the analysis and education topics presented to patients. Basic demographic data (including age, race, sex, rank and branch of service) will be collected at the time of interview and used for future

analysis. This information will be used at the end of data collection to determine if the target population is truly representative of the overall MAMC population. Medications will then be reviewed with the patient, with information provided by the pharmacist or lead investigator regarding the status and care of the medication. Patients will be advised of any medication that is past its' proper expiration date, that appears to be a conflicting medication with their known medical history, or has been stored improperly and has been rendered ineffective. The visiting staff will advise patients on how to safely remove these medications from the home and return them to the MAMC pharmacy for proper disposal. Educational materials on appropriate storage and care of medications have been previously written by the MAMC pharmacy staff and will be reviewed and left with the patient prior to completion of the home visit. Once collected during the home visit, the medication list will be compared with their Medication Profile Index (MPI) as contained on the Computerized Health Care System (CHC) at the MAMC. Discrepancies will be noted, recorded and medication profiles updated, ensuring that their primary care providers have an up-to-date list of their patients' medications in their medical records. Medications obtained appropriately from non-military health care establishments will be identified and the information updated in their military MPI. The lead investigator will collect data regarding the number of medications used, type and name of medication, prescription status, expiration status, and intention to use for a future date. Information will be recorded as percentages for prescription status, expiration status, and intention use at a Future date. For example, the number of prescription or non-prescription medications will be compared to the total number of prescriptions to develop a percentage value. The lead investigator will manually collect and analyze data with the assistance of the support staff.

**Progress:** This protocol recently received approval. Work has not yet begun.



## **Detail Summary Sheets**

### **Cardiology Service, Department of Medicine**

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 99/053

**Status:** Ongoing

**Title:** Multinational, Multicenter, Double-Blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-Term Treatment with Valsartan, Captopril, and Their Combination in High-Risk Patients After Myocardial Infarction

**Principal Investigator:** LTC James J. King, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** COL Alice M. Mascette, MC; MAJ James P. Olson, MC; LTC David T. Schachter, MC; CPT Kenneth M. LeClerc, MC; MAJ Steven E. Miller, MC; LTC Michael J. Wilson, MC

**Keywords:** Myocardial infarction, valsartan, captopril, mortality

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Apr 03

**Periodic Review:**  
4/23/2002

**Study Objective:** (1) To demonstrate that long-term administration of valsartan is more effective than captopril in reducing total mortality after acute myocardial infarction, (2) To demonstrate that long-term administration of the combination of valsartan with captopril is more effective than captopril alone in reducing total mortality after acute myocardial infarction, and (3) If valsartan as monotherapy cannot be shown to be superior to captopril as in objective 1, to demonstrate that long-term administration of valsartan given as monotherapy is at least as effective as captopril given as monotherapy in reducing total mortality after acute myocardial infarction.

**Technical Approach:** VALIANT is a prospective multinational, multicenter, double-blind, randomized, active-controlled phase III study with three parallel treatment groups. The three treatment groups are 1) Captopril monotherapy (active control drug). The target dose is 50 mg three times daily; 2) Valsartan monotherapy (investigational drug). The target dose is 160 mg twice daily; 3) The combination of captopril and valsartan (investigational regimen). The target doses are 50 mg three times daily and 80 mg twice daily, respectively. The study consists of two phases: 1) a study medication initiation and titration phase and 2) maintenance phase. The duration of these two phases depends upon the patient's status and response to study medication. Randomization and initiation of study medication will occur at Visit 1 on Day 1. For most patients, this will occur in hospital. Dose titration and maintenance will occur at Visits 2-16. Visit 2 will occur on Day 15 or at hospital discharge, whichever is first. For patients not in hospital at the time of randomization, Visit 2 will occur on Day 15. Visits 3-16 are planned as outpatient visits, but depending on the patient's status, may occur in hospital. They are to be performed at specified time points but some flexibility is allowed. During the first year, visit may take place up to 15 days before or after the protocol-scheduled visit. Telephone follow-up is permitted if the patient cannot come for follow-up visits. The study will end when the required number of primary endpoints has been reached. This may occur prior to or after Month 48. If the study ends prior to Month 48, the procedures listed for Visit 16 will be completed for all patients. If the study is extended beyond Month 48, the procedures listed for Visit 15 will be completed every 4 months until study end, at which point the procedures listed for Visit 16 will be completed.

**Progress:** A total of 8 patients were enrolled in this study at MAMC. One patient withdrew consent after receiving study medication and seven patients were still being followed during FY02. This study is closed to enrollment but remains ongoing to continue patient follow-up.



### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/062                 | <b>Status:</b> Terminated            |
| <b>Title:</b> Substudy 02: The Neurohormone Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction   |  |                                      |
| <b>Principal Investigator:</b> LTC James J. King, MC  |  |                                      |
| <b>Department:</b> Medicine/Cardiology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC  |  |                                      |
| <b>Keywords:</b> VALIANT Valsartan neurohormone substudy 2  |  |                                      |
| <b>Start Date:</b><br>4/25/2000   | <b>Est. Completion Date:</b><br>Apr 03 | <b>Periodic Review:</b><br>4/12/2002 |
| <b>Study Objective:</b> To determine the effect of valsartan, captopril, and the combination of valsartan and captopril on the levels of neurohormones, measures of oxidative stress, and inflammation (plasma catecholamines, aldosterone, brain natriuretic peptide, aldehydes, adrenomedullin, collagen one telopeptide, procollagen type III, Nterminal propeptide, and C-reactive protein) at baseline, one month and 20 months post infarction, and with each episode of congestive heart failure requiring hospitalization and to assess the relationships between post-infarction neurohormonal activation, cardiovascular risk factors, and clinical outcome and evaluate the effect of valsartan, captopril and their combination on these relationships. |  |                                      |
| <b>Technical Approach:</b> This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of neurohormones as an indicator of prognosis for patients suffering from myocardial infarction. Blood samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, blood samples will be taken whenever the patient is hospitalized for heart failure. Samples will be sent to a central laboratory for evaluation.   |  |                                      |
| <b>Progress:</b> This study has been terminated by principal investigator, effective 12 Apr 02, as no patients have been enrolled in this study within the last 12 months. Only two patients enrolled in this substudy at MAMC.   |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/063 | <b>Status:</b> Terminated |
|------------------------|------------------------|---------------------------|

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**Title:** Substudy 04: The Microalbuminuria Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction

**Principal Investigator:** LTC James J. King, MC

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| <b>Department:</b> Medicine/Cardiology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC

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**Keywords:** VALIANT Valsartan microalbuminuria substudy 4

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**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Apr 03

**Periodic Review:**  
4/12/2002

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**Study Objective:** To assess the relationship between microalbuminuria and prognosis, and evaluate how valsartan and captopril modify this relationship and whether a correlation between microalbuminuria, neurohormonal activation and gene polymorphisms exists.

**Technical Approach:** This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of albuminuria as an indicator of prognosis for patients suffering from myocardial infarction. Spot urine samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, urine samples will be taken whenever the patient is hospitalized for heart failure. Urine samples will be sent to a central laboratory for evaluation.

**Progress:** This study has been terminated by principal investigator, effective 12 Apr 02, as no patients have been enrolled in this study within the last 12 months. Only two patients enrolled in this substudy at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/042                  | <b>Status:</b> Ongoing              |
| <b>Title:</b> The Coreg Heart Failure Registry: COHERE   |  |                                     |
| <b>Principal Investigator:</b> LTC James J. King, MC   |  |                                     |
| <b>Department:</b> Medicine/Cardiology   |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ James P. Olson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC            |  |                                     |
| <b>Keywords:</b> Heart failure, registry, mortality, hospitalization, concomitant medications, global assessment, NYHA class |  |                                     |
| <b>Start Date:</b><br>2/23/1999  | <b>Est. Completion Date:</b><br>Jun 99 | <b>Periodic Review:</b><br>1/4/2002 |

**Study Objective:** (1) To collect clinically pertinent outcome data (e.g., mortality, need for hospitalization, use of concomitant medications, patient global assessment, NYHA class in patients with heart failure) receiving Coreg under the care of a broad population of community physicians, (2) To compare the clinical characteristics of the patients treated in the US Phase III and early extended physician use programs with those treated in the community and to assess outcome differences in major subpopulations, (3) To characterize the experience with initiation of Coreg in the community, and (4) To compare patient characteristics and management approaches between cardiologists and internists.

**Technical Approach:** The Coreg Heart Failure Registry will document the relationship of selected patient characteristics to outcomes, such as morbidity, mortality, need for hospitalizations, quality of life and change in clinical status as well as tolerability. By the year 2000, COHERE will contain the most up-to-date information on the natural history of, and effect of B-Blockade in CHF. COHERE will involve approximately 600 participating physicians, and will enroll 6,000 patients with heart failure receiving Coreg. The live portion of the registry will take place over 30 months, and patients will be assessed over a period of 24 months.

**Progress:** A total of 31 patients enrolled in this study at MAMC, with no patients enrolled during FY02. There was 1 patient that screen failed, 30 patients completed the study. This study is closed to enrollment and in the process of being closed out by the study sponsor.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/300 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** CardioSEAL Septal Occlusion System (HUD)

**Principal Investigator:** LTC David T. Schachter, MC

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**Department:** Medicine/Cardiology

**Facility:** MAMC

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**Associate Investigator(s):** None.

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**Keywords:** HUD, septal occlusion, recurrent cryptogenic stroke, CardioSEAL Septal Occlusion System

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**Start Date:**

1/22/2002

**Est. Completion Date:**

Dec 04

**Periodic Review:**

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**Study Objective:** Humanitarian Use Device

**Technical Approach:** The CardioSEAL Septal Occlusion System is approved as an HUD for the indication of patent foramen oval closure (PFO). MAMC investigators trained to deploy this device must submit certificates of training and updated curriculum vitae to the Chairman, IRB. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** No patients have received the device at Madigan. On 17 Oct 2002 we plan to insert the device into the first two patients.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/300                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Jostent Coronary Stent Graft (HUD)  |  |                                      |
| <b>Principal Investigator:</b> LTC David T. Schachter, MC                                       |  |                                      |
| <b>Department:</b> Medicine/Cardiology  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Bruce R. Kenwood, MC                                      |  |                                      |
| <b>Keywords:</b> coronary stent graft, HUD, arterial perforations, Jostent Coronary Stent Graft |  |                                      |
| <b>Start Date:</b><br>9/25/2001   | <b>Est. Completion Date:</b><br>Sep 10 | <b>Periodic Review:</b><br>8/27/2002 |

**Study Objective:** Humanitarian Use Device

**Technical Approach:** The Jostent Coronary Stent Graft is approved as an HUD for the indication of arterial perforation. Physicians trained to deploy the stent will be added as associate investigators upon receipt of documentation of training. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** This is a HUD device used for emergency bailout of a coronary perforation. We have not had to put in any of these stents.

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/056      **Status:** Completed

**Title:** A Multi-Center, Six-Month, Double-Blind, Placebo-controlled, Parallel-group design Clinical Study to Assess the Efficacy and Safety of a Daily Oral Dose of 125 mg of Azimilide Dihydrochloride for the Prophylactic Treatment of Atrial Fibrillation and an Open-label follow-up Clinical Phase to Assess the Long-term Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride

**Principal Investigator:** LTC Michael J. Wilson, MC

**Department:** Medicine/Cardiology      **Facility:** MAMC

**Associate Investigator(s):** LTC James J. King, MC; LTC David T. Schachter, MC; MAJ Rosemary P. Peterson, MC

**Keywords:** AFIB, Atrial Fibrillation, Azimilide, CHF, IHD

**Start Date:**  
1/23/2001

**Est. Completion Date:**  
Dec 04

**Periodic Review:**  
1/8/2002

**Study Objective:** Primary: To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in prolonging the tachycardia-free period in 2 patient strata separately in: Patients with CHF and/or IHD and, Patients with neither CHF nor IHD. Secondary: (1) To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the total number of symptoms (among 6 pre-specified symptoms from the Event Symptom Severity Checklist) reported during the first symptomatic event, (2) to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the frequency of symptomatic events (i.e., an assessment of efficacy that allows for multiple events per patient), (3) to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the total SVA burden in patients. The SVA burden includes the frequency, duration, and severity of AFib, AFLut, or PSVT events, (4) to assess the impact of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in patient quality-of-life, specifically, on the physical functioning subscale of the SF-36 at week 4, and (5) To assess the number of days in-hospital and number of emergency room visits due to AFib, AFLut, or PSVT events following initial discharge for patients hospitalized for the loading period, and beginning on Day 1 for all other patients.

**Additional Objectives:** To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in prolonging the tachycardia-free period in patients with and without CHF/IHD (i.e., and assessment of efficacy that combines time to first symptomatic event information from both strata) To assess individual symptoms from the Brignole Atrial Fibrillation Symptom Checklist (week 4) To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the number of asymptomatic events To assess the safety of 125mg of Azimilide Dihydrochloride in patients both with and without CHF/IHD (strata combined). Safety will be assessed by examining the type and incidence of AEs, ECG parameters, and type and severity of laboratory abnormalities and chest x-ray results

**Open Label, Follow-up Phase:** Assess the safety of outpatient once-daily initiation of 125mg of Azimilide Dihydrochloride in patients who received placebo and who complete the doubleblind, placebo-controlled study Assess the long-term safety of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study Assess the long-term efficacy (i.e.: frequency of SVA events) of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study.

**Technical Approach:** This is a randomized, six-month, double-blind, placebo-controlled, multi-center, parallel group design phase, to assess the efficacy and safety of 125mg of daily oral dose of Azimilide Dihydrochloride in maintaining sinus rhythm in patients who have had symptomatic AFib documented by TTM or ECG during the 1 month screening period. An open label phase,

designed to evaluate the long-term safety of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind portion follows. Approximately 660 patients will be enrolled at 80-100 sites. Patients will be stratified according to whether or not they have a history of CHF and/or IHD, then randomly assigned to the 2 treatment groups of 2 strata. Enrollment will be stopped once 440 patients with CHF/IHD have been randomized. Enrollment of patients without CHF/IHD will be stopped once 220 of those patients are randomized or enrollment of CHF/IHD patients has been completed. A separate randomization schedule will be used for patients with NYHA Class III CHF. This is being done to ensure as much as possible that an equal number of patients with Class III CHF receive of Azimilide Dihydrochloride and placebo. Patients will be evaluated at Baseline/Day 1, day 4, and weeks 2, 4, 6, 8, 10, 12, and 26. Throughout the double-blind phase, patients will use a TTM device to transmit their ECGs: If they experience symptoms that they believe are indicative of an arrhythmia, and daily thereafter until they return to sinus rhythm and when contacted weekly by the central monitoring service. Patients will complete the Short Form 36 (SF 36) quality-of-life questionnaire and the Brignole Atrial Fibrillation Symptom Checklist. These forms will be completed at the day 1 visit prior to dosing in the hospital (baseline), and for weeks 4, 12 and 26 visits. Patients will only be allowed to enter the screening period while in sinus rhythm. Females of childbearing age will be given the special issues leaflet regarding pregnancy. Patients will be asked to record and send a transmission to the central TTM service any time they experience symptoms they believe are indicative of an arrhythmia. This monitoring will occur over a 1-month period, and patients may continue their antiarrhythmic medications at the investigator's discretion. Patients may be randomized into the double-blind phase upon return to sinus rhythm from their qualifying event of AFib. Patients who fail the 1-month screening period and who are taking their antiarrhythmic medications may discontinue those medications and repeat the 1-month screening period one time. Patients may qualify during the screening period with any ECG-documented symptomatic AFib. The qualifying ECG will be forwarded to the central facility if it was not obtained by TTM. Patients must have their Day I visit within 30 days of the onset of the documented symptomatic AFib event of the screening phase. The Base line visit must occur within 7 days prior to the first dose of study drug. Loading period in patients with (inpatient) and without (outpatient) CHF/IHD: Patients with CHF or IHD will be monitored in the hospital during the 3-day loading period. After all Baseline and Day 1 procedures have been completed and the patient is confirmed to be in sinus rhythm, patients with and without CHF/IHD will take the first dose of the 3-day, twice daily, loading regimen in the presence of study staff. For the remainder of the 3 days, patients will take the study medication twice daily. Thereafter for the remainder of the study, all patients will take study medication once daily at the same time every day. Patients will be considered to have completed the double-blind portion of the study when they have a sinus rhythm-containing day after their second confirmed occurrence of symptomatic AFib, AFlut, or PVST event or after they complete 26 weeks. Patients who complete the double-blind study will be given the opportunity to enter the open label follow-up phase. Open Label, Follow-up Phase: Patients may begin this phase of once-daily oral dose of 125mg of Azimilide Dihydrochloride the day following their completion of the double-blind study. Patients will have visits every 2 weeks for the first 12 weeks. After that, patients will return at weeks 26, 38, 52, and every 26 weeks thereafter, for approximately 2 years. During the open label phase, the TTM will not be used to transmit ECGs, but patients may return to the clinic if they experience symptoms of their arrhythmia. Patients will return to the study site after 7 days ( $\pm$ 1 day) for a 12-lead ECG. Patients who are in sinus rhythm will undergo scheduled evaluations, return home, and continue routine followup care. Patients who choose to enter the open label phase will have visits at weeks 1, 2, and every 2 weeks for the remainder of the first 12 weeks. They will return at weeks 26, 38, 52 and then every 26 weeks thereafter until approximately 2 years from the time the patient completes the double-blind study. Patients who complete or withdraw from the double blind or open label phases will return to the clinic for follow-up visits and 30 days post-treatment.

**Progress:** The study sponsor closed MAMC as a study site, effective 27 Mar 02, due to lack of enrollment. No subjects enrolled at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/055      **Status:** Completed

**Title:** A Six-Month, Multi-Center, Double-Blind, Placebo-controlled, Parallel-group Design Clinical Study to Assess the Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride for the Treatment of Atrial Fibrillation in Patients Who Require Electrical Cardioversion with an Open-label Follow-up Phase to Assess the Long-term Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride

**Principal Investigator:** LTC Michael J. Wilson, MC

**Department:** Medicine/Cardiology      **Facility:** MAMC

**Associate Investigator(s):** LTC James J. King, MC; LTC David T. Schachter, MC; MAJ Rosemary P. Peterson, MC

**Keywords:** Atrial Fibrillation, Afib, Azimilide, Cardioversion

**Start Date:**  
1/23/2001

**Est. Completion Date:**  
Dec 04

**Periodic Review:**  
1/8/2002

**Study Objective:** Primary: to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in prolonging the time from the start of the efficacy period to the first symptomatic or asymptomatic AFib, AFLut, or PSVT event. The efficacy period begins following a three day, twice daily oral dose of study medication after sinus rhythm has been documented as a result of successful cardioversion (DC or Spontaneous) on Day 4 (+2 days). An event is defined as: AFib, AFLut, or PVST <24 hours duration for which the patient is readmitted to the hospital or requires DC cardioversion, or AFib, AFLut, or PVST of  $\geq 24$  hours duration. Secondary: to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo: (1) On successful DC cardioversion from AFib (Day 4, +2days), (2) On "symptom frequency load," during the first AFib, AFLut, or PSVT event, (3) On the quality-of-life measure referred to as physical functioning on the SF-36, (4) On individual symptoms from the Brignole Atrial Fibrillation Symptom Checklist, (5) On the number of days spent in-hospital or as emergency room visits due to AFib, AFLut, or PVST events following initial discharge on day four. Open Label, Follow-up Phase: Assess the safety of outpatient once-daily initiation of 125mg of Azimilide Dihydrochloride in placebo patients who complete the double-blind, placebo-controlled study, assess the long-term safety of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study, assess the efficacy of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study.

**Technical Approach:** This is a randomized, double-blind, placebo-controlled, six-month, multi-center, parallel group design study, followed by an open-label, follow-up phase to assess the efficacy and safety of 125mg of daily oral Azimilide Dihydrochloride. Approximately 440 patients will be enrolled at 60-80 sites. The number of patients per site is to be assessed on an ongoing basis by the sponsor. Recruitment is expected to last 9-12 months. Patients who are in AFib and in need of a DC cardioversion will be hospitalized and randomized to receive a twice weekly oral dose of 125mg Azimilide Dihydrochloride or placebo for 3 consecutive days. Beginning on Day 4, patients will receive a once-daily oral maintenance dose of their assigned treatment until they complete or withdraw from the double-blind study. During the hospitalization, patients will be monitored by telemetry. A 12-lead ECG will be obtained prior to the first dose on all days while in the hospital. All patients will be re-assessed by 12-lead ECG on Day 4 (or within the following 2 days) prior to taking study medication that day. Patients who are in sinus rhythm prior to DC cardioversion on day 4 (+2 days) will be considered to have spontaneously cardioverted (after sinus rhythm has been documented by two 12-lead ECGs taken at least one hour apart). Patients who have not cardioverted to sinus rhythm by Day 4 (+2 days) will undergo a DC cardioversion. On the day of cardioversion, all study medication will be withheld until successful cardioversion has been



documented. Patients who have not achieved successful cardioversion on Day 4 (+2 days) will be withdrawn from the study. Once the patient is successfully cardioverted, AFib, AFlut, or PVST recurrences must be documented electrocardiographically (12-lead ECG preferred). The duration of the recurrence will be documented by the patient's own recollection and subsequent follow-up. At all visits in the treatment period of the double-blind, study (except day 4), patients will be asked if they have been hospitalized or required an emergency room visit for any reason. For patients to remain in the study, sinus rhythm should be restored within 8 weeks of their event. Documentation must be obtained by any means of electrocardiograph tracing immediately after cardioversion and again by 12-lead ECG at least one hour later. If sinus rhythm is not restored within 8 weeks, patients must be withdrawn from the study. Patients will have additional scheduled visits during the double-blind study at weeks 2, 4, 6, 8, 10, 12, and 26. The coordinator/investigator should instruct the patient to return to the site for unscheduled visits if they experience symptoms of their arrhythmia, or any unusual symptoms, infection, nonspecific fevers, pharyngitis, or influenza-like symptoms. Patients will complete the Short Form 36 (SF 36) quality-of-life questionnaire and the Brignole Atrial Fibrillation Symptom Checklist. Patients will be considered to have completed the double-blind portion of the study upon documentation of the second AFib, AFlut, or PVST event or after they complete 26 weeks. Patients who complete the double-blind study will be given the opportunity to enter the open label follow-up phase. Open Label, Follow-up Phase: Patients may begin this phase of once-daily oral dose of 125mg of Azimilide Dihydrochloride the day following their completion of the double-blind study. Upon entry into the open label phase, patients will be given sufficient Azimilide Dihydrochloride for 8 days. Patients will return to the study site after 7 days ( $\pm 1$  day) for a 12-lead ECG. Patients who are in sinus rhythm will undergo scheduled evaluations, return home, and continue routine follow-up care. Patients who choose to enter the open label phase will have visits at weeks 1, 2, and every 2 weeks for the remainder of the first 12 weeks; they will then return at weeks 26, 38, 52, and then every 26 weeks (6 months) thereafter until approximately 2 years from the time the patient completes the double-blind study. Patients who complete or withdraw from the either phase will return to the clinic for followup visits 7 and 30 days post-treatment.

**Progress:** The study sponsor closed MAMC as a study site, effective 27 Mar 02, due to lack of enrollment. No subjects enrolled at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 96/069      **Status:** Ongoing

**Title:** Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

**Principal Investigator:** LTC Michael J. Wilson, MC

**Department:** Medicine/Cardiology      **Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick A. Cambier, MC; COL Roger F. Chamusco, MC; COL Alice M. Mascette, MC; MAJ Herman E. Collier III, MC; LTC Karl C. Stajduhar, MC; MAJ Michael D. Eisenhauer, MC; CPT John A. McHenry, MC; MAJ Maureen A. Arendt, MC; CPT Thomas M. Roe, MC; MAJ James P. Olson, MC

**Keywords:** Atrial fibrillation, drug therapy, heart rate control, heart rhythm control

**Start Date:**  
2/16/1996

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
1/8/2002

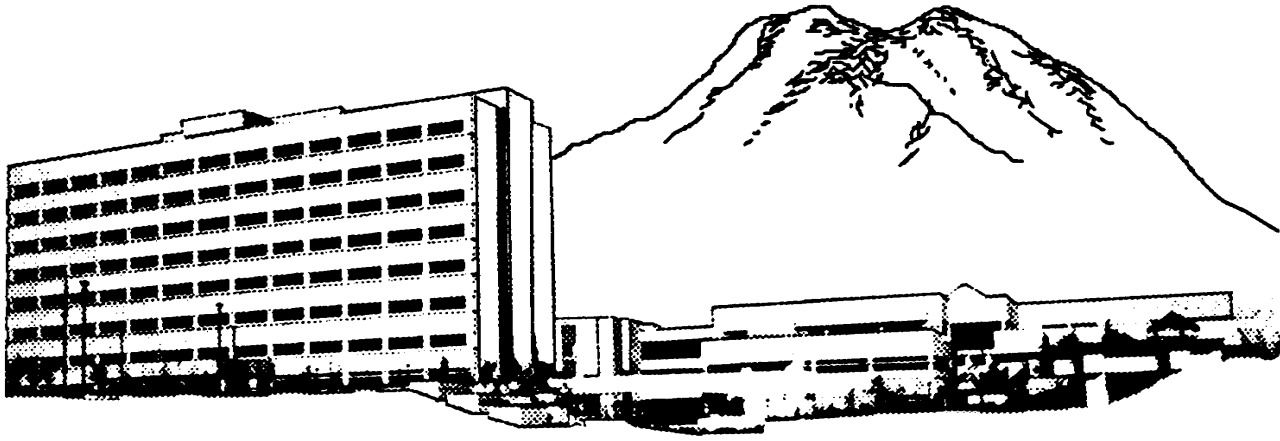
**Study Objective:** 1) To compare whether optimized antiarrhythmic drug therapy administered to attempt to maintain sinus rhythm has an impact on total mortality when compared to optimized therapy which controls the heart rate. 2) Since stroke is such an important endpoint in trials of patients with atrial fibrillation, composite endpoints will include the following: total mortality, disabling stroke or anoxic encephalopathy, major bleeding and cardiac arrest; cost; quality of life.

**Technical Approach:** This is a multi center trial sponsored by the National Heart, Lung, and Blood Institute. The purpose is to compare the effect on survival of two different treatment plans in patients with atrial fibrillation. One treatment is aimed at rate control and the other at maintaining a normal sinus rhythm. The primary physician will choose which drug or drugs are used to obtain each treatment objective. The physician will initially determine the treatment to convert patients to normal sinus rhythm after which the patient will be randomized to one of the treatments described above. Patients will be followed at month 2 and 4 and then at least every 4 months until the year 2001. Patients will complete a quality of life questionnaire and have an assessment of their functional status completed at various time points. Patients who fail their assigned treatment or are intolerant will continue to be followed regardless of crossover to another therapy. We anticipate enrolling 15 patients at Madigan Army Medical Center.

**Progress:** A total of 29 patients enrolled into this study at MAMC, with no patients enrolled during FY02. All 20 received study drug, there were 2 patients lost to follow-up. 6 patients died while on the study, these deaths were all considered unrelated to study participation. The remaining 21 patients all completed follow-up. This study is closed to enrollment and the sponsor is in the process of closing this study out. (Note: last year's report of 32 patients enrolled was an administrative error).

## Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/110                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Efficacy and Safety Study of the Oral Direct Thrombin Inhibitor H 376/95 Compared with Dose-adjusted Warfarin (Coumadin) in the Prevention of Stroke and Systemic Embolic Events in Patients with Atrial Fibrillation (SPORTIF V)   |  |                                      |
| <b>Principal Investigator:</b> LTC Michael J. Wilson, MC  |  |                                      |
| <b>Department:</b> Medicine/Cardiology  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC David T. Schachter, MC; LTC James J. King, MC; MAJ Rosemary P. Peterson, MC; COL Frederick G. Flynn, MC   |  |                                      |
| <b>Keywords:</b> thrombin inhibitor, warfarin, coumadin, stroke, atrial fibrillation  |  |                                      |
| <b>Start Date:</b><br>7/25/2000   | <b>Est. Completion Date:</b><br>Sep 02 | <b>Periodic Review:</b><br>6/25/2002 |
| <b>Study Objective:</b> (1) To determine whether H 376/95 is non-inferior compared to dose-adjusted warfarin aiming for an INR 2.0-3.0 for the prevention of all strokes (fatal and nonfatal) and systemic embolic events in patients with chronic non-valvular AF, (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for an INR of 2.0-3.0 for the combined endpoint of prevention of death, nonfatal strokes, nonfatal systemic embolic events and nonfatal acute myocardial infarction (AMI), (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for INR 2.0-3.0 for the combined endpoint of prevention of ischemic strokes, TIAs and systemic embolic events, and (3) To assess the safety of H 376/95 compared to dose-adjusted warfarin aiming for INR 2.0-3.0 with an emphasis on major and minor bleeding events and any treatment discontinuations.  |  |                                      |
| <b>Technical Approach:</b> This is a multicenter, randomized, double-blind, two arm, parallel group study comparing the effects of H 376/95 versus dose-adjusted warfarin. Subjects will be followed for at least one year, up to 2 1/2 years. Eligible patients will be randomized and stratified according to current low dose aspirin use and previous stroke or TIA history. Subjects will complete a 2 week screening period prior to randomization to receive either H 376/95 36 mg bid (and placebo for warfarin) or to dose-adjusted warfarin (and placebo for H 376/95). Screening will include consent process, medical history, vital signs, ECG, blood/urine samples and physical examination. Upon randomization, a second ECG will be performed, and the Stroke Symptom Questionnaire will be completed. Study visits will be performed at weeks 1, 4, 6, and then months 2, 3, 4, 5, 7, 8, 10, 12 and then every 3 months thereafter until the study treatment is completed. At study visits, study medication will be returned and new drug will be dispensed, concomitant medications and adverse events will be reviewed, safety blood samples and melagatran samples will be obtained. INR samples will be obtained as necessary. At months 6, 12, 18, and 24 visits subjects will undergo the above tests in addition to ECGs and the Stroke Symptom Questionnaire. Subjects will be contacted by telephone at months 7, 9, and 11 and will be required to return to the clinic for in-clinic INR evaluation as necessary. At the end of the study subjects will have a complete PE, vital signs, ECG, blood tests, INR samples, and the Stroke Symptom Questionnaire will be obtained. Following treatment withdrawal, the subjects will be followed an additional 2 weeks until satisfactory conversion from blinded study therapy to normal active treatment has been made. Subjects will return to the clinic for INR draws using a sponsor provided CoaguChek System. INR values will remain blinded to the investigator and study coordinator utilizing the CoaguChek System and the IVRS system. |  |                                      |
| <b>Progress:</b> A total of 21 patients were enrolled into this study here at MAMC, with 6 patients being enrolled since Oct 01. Twelve patients screen failed, 2 patients withdrew consent before receiving study drug, and 1 patient withdrew consent after receiving study drug. 6 patients remain in follow-up. This study is closed to patient enrollment here at MAMC.  |  |                                      |



## **Detail Summary Sheets**

### **Gastroenterology Service, Department of Medicine**

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/031                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> The Use of a Nutritional Supplement as an Antimicrobial in Helicobacter pylori Eradication  |  |                                      |
| <b>Principal Investigator:</b> MAJ Robert K. Durnford, MC   |  |                                      |
| <b>Department:</b> Medicine/Gastroenterology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> James R. Wright, BA, MT (ASCP); LTC Spencer S. Root, MC; MAJ William K. Hirota, MC; Janet C. Chilton; LTC Jonathan P. Kushner, MC |  |                                      |
| <b>Keywords:</b> Helicobacter pylori,, nutritional supplements, garlic  |  |                                      |
| <b>Start Date:</b><br>1/25/2000   | <b>Est. Completion Date:</b><br>Dec 01 | <b>Periodic Review:</b><br>2/26/2002 |

**Study Objective:** To assess the antimicrobial action of garlic on Helicobacter pylori: to attempt to eradicate Helicobacter pylori with the combination of garlic and a proton-pump inhibitor in a double-blinded, placebo-controlled trial; also, to assess changes in symptoms, endoscopic appearance, histology, quantitative cultures, quantitative urease activity (by breath test) and serum and gastric tissue cytokines following the eradication attempt.

**Technical Approach:** After screening up to 500 candidates with H. pylori serology, as well as a standardized GI Likert (17) scale dyspepsia symptom questionnaire and a food frequency questionnaire, two 7 mL red top blood tubes (one for H pylori serology and one for cytokine assays) and one complete blood count will be drawn at the time of the initial screening. Those with positive serology will be asked to discontinue PPI, and if possible, non-steroidal antiinflammatory medications. Active H. pylori infection will be confirmed in patients with positive serology by the presence of either positive H. pylori on histology and a positive rapid urease test. At endoscopy, after aspiration of gastric juice, seven biopsies will be obtained from the antrum, and seven from the body of the stomach. One biopsy from each will be used for the RUT test, with two for histology and two for H. pylori culture. The sixth biopsy will be frozen in liquid nitrogen for cytokine mRNA expression and the seventh biopsy, as well as the gastric aspirate, assayed for cytokine protein. Patients positive for h. pylori infection will be stratified into either a low/normal habitual garlic consumption. Patients will be blocks of 15 Those in the treatment blocks will receive three garlic supplement capsules twice daily while those in the placebo blocks will receive six identically appearing capsules. Patients will refrain from antibiotic, PPI, bismuth, and if possible, NSAID use during this period. Blood work and endoscopy will be repeated for purposes of research and data collection.

**Progress:** Subject recruitment for this study has been completed. Protocol remains ongoing to continue follow-up of enrolled subjects. MAJ Durnford assumed the role of PI due to the retirement of its original PI, LTC Kushner.

### Detail Summary Sheet

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|                        |                        |                        |
|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/016 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Evaluation of Fecal Lactoferrin Levels of Inflammatory Bowel Disease and Irritable Bowel Syndrome Patients

**Principal Investigator:** MAJ Steven D. Mahlen, MC

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|   |                       |
|---|-----------------------|
| <b>Department:</b> <del>Medicine/Gastroenterology</del> Pathology | <b>Facility:</b> MAMC |
|---|-----------------------|

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**Associate Investigator(s):** MAJ Robert K. Durnford, MC; CPT Charles L. Scott, MC; LTC David K. Turgeon, MC; COL Jerome B. Myers, MC; MAJ Anne L. Champeaux, MC; Dawn M. Swimm, ARNP

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**Keywords:** Inflammatory bowel disease, irritable bowel syndrome, fecal lactoferrin

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**Start Date:**  
11/27/2001

**Est. Completion Date:**  
Dec 02

**Periodic Review:**  
10/21/2002

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**Study Objective:** The objectives of this study include: (1) to determine the fecal lactoferrin levels in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) patients in various stages of disease; (2) to assess inter-patient fecal lactoferrin levels; (3) to assess patients suspected of having IBS and compare their fecal lactoferrin levels to in-house evaluation procedures; and (4) to compare disease activity to levels of fecal lactoferrin.

**Technical Approach:** A total enrollment of 140 patients will be used in the study, comprised of the following groups: 40 patients (20 males and 20 females) with a documented history of Crohn's disease and current large bowel or small bowel involvement, 40 patients (20 males and 20 females) with a documented history of ulcerative colitis, 40 patients (12 males and 28 females) with a documented history of IBS, and 20 patients suspected of having IBS or IBD. All of the patients will be, or have been, evaluated for gastrointestinal illnesses at the Gastroenterology Clinic using in-house methods. In addition, stool samples from all of the patients will be collected and tested by the IBD-SCAN and IBD-CHEK methods according to the manufacturer for detection of fecal lactoferrin. Also, stool samples from 20 patients suspected of having either IBS or IBD will be tested for bacterial fecal pathogens, Clostridium difficile antigen and toxin A, and ova and parasites using standard microbiology procedures.

**Progress:** During FY02, a total of 10 patients were enrolled in this study at MAMC and gave stool specimens for fecal lactoferrin testing. Fecal lactoferrin levels will be evaluated when more patients are enrolled; the test is best performed in large batches.

### Detail Summary Sheet

|  |  |                                       |
|--|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 97/012                  | <b>Status:</b> Completed              |
| <b>Title:</b> A Pre-Clinical Research and Development Study to Evaluate Stool Specimens for the PolyStat™ CRC Test |  |                                       |
| <b>Principal Investigator:</b> COL Amy M. Tsuchida, MC   |  |                                       |
| <b>Department:</b> Medicine/Gastroenterology   |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> LTC Robert H. Sudduth, MC; MAJ Kazunori Yamamoto, MC; MAJ John G. Carrougher, MC |  |                                       |
| <b>Keywords:</b> Cancer:colon, colon tunor antigen, CoTA test strip  |  |                                       |
| <b>Start Date:</b><br>11/15/1996   | <b>Est. Completion Date:</b><br>Oct 97 | <b>Periodic Review:</b><br>10/23/2001 |

**Study Objective:** Evaluate the clinical utility potential of the PolyStat™ CRC Test strip assay in detecting basement membrane complexes in individuals with or without colorectal cancer, respectively. And to isolate sufficient amounts of colon BMC for additional antibody production and antigen characterization using the PolyStat™ CRC Teststrip assay and other antibody tests.

**Technical Approach:** This is a multicenter trial with MAMC providing stool specimens from patients undergoing colonoscopy. Following colonoscopy, eligible participants will be instructed to collect a stool specimen after their stools have returned to normal and prior to any other intestinal procedures. The specimen will be shipped directly to Alidex Diagnostic Sciences, Inc.

**Progress:** 217 subjects enrolled in this study at MAMC, with 201 patients completing all study procedures. 16 patients were dropped from the study because they had not returned their stool specimens. Preliminary findings and results are not yet available. This study was closed at MAMC, Aug 02, due to the retirement of the principal investigator.

### Detail Summary Sheet

|                        |                        |                          |
|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/144 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** A Randomized, Double-blind, Placebo-controlled, Dose Finding, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Tegaserod Given Orally at Three Dose Levels and Placebo in Patients with Functional Dyspepsia and Documented Delayed Gastric Emptying

**Principal Investigator:** COL Amy M. Tsuchida, MC

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert K. Durnford, MC; MAJ Eric J. Ormseth, MC; LTC Jonathan P. Kushner, MC

**Keywords:** Zelmec, tegaserod, placebo, functional dyspepsia, delayed gastric emptying

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Oct 01

**Periodic Review:**  
9/25/2001

**Study Objective:** (1) To determine in patients with symptoms of dyspepsia and documented delay in gastric emptying rate the efficacy of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo as measured by satisfactory relief of meal related upper stomach problems and (2) to rate the effects of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo; (3) patient's assessment of symptoms of functional dyspepsia; (4) patient's quality of life and (5) the safety and tolerability.

**Technical Approach:** This is a multicenter, Phase II dose-finding trial with a parallel group design in patients with functional dyspepsia and delayed gastric emptying as measured by scintigraphy. Following a one week screening and a two week washout period, eligible subjects will be randomized to receive either placebo tid or daily doses of 1.5 mg, 6 mg or 18 mg Zelmec (tegaserod) given orally tid for 8 weeks. Data will be collected on patient symptoms of dyspepsia and quality of life. Drug compliance, concomitant medications and adverse events will be monitored.

**Progress:** This study was closed to enrollment, 15 Apr 02 per the study sponsor. No patients enrolled in this study at MAMC.



### Detail Summary Sheet

|   |  |                                       |
|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 98/004                  | <b>Status:</b> Completed              |
| <b>Title:</b> Epidemiology of Barrett's Esophagus   |  |                                       |
| <b>Principal Investigator:</b> COL Amy M. Tsuchida, MC  |  |                                       |
| <b>Department:</b> Medicine/Gastroenterology  |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> Diana C. Farrow, Ph.D.; MAJ William K. Hirota, MC; LTC Spencer S. Root, MC; LTC Robert H. Sudduth, MC |  |                                       |
| <b>Keywords:</b> Barrett's esophagus, epidemiology, GERD  |  |                                       |
| <b>Start Date:</b><br>10/17/1997  | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>10/23/2001 |

**Study Objective:** To determine whether there are any specific environmental, dietary, or personal factors which increase the risk of developing Barrett's Esophagus.

**Technical Approach:** Patients who are undergoing an upper endoscopy for evaluation of their heartburn complaints will have four biopsies and a small amount of stomach fluid taken for research purposes. Information from the endoscopic findings will be abstracted from medical records.

**Progress:** This study was reported as completed at MAMC, 5 Jun 02. 128 patients consented and all completed study procedures. No adverse events were reported. Preliminary data is not yet available.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 96/164      **Status:** Completed

**Title:** Epidemiology of Gallbladder Sludge and Stones in Pregnancy

**Principal Investigator:** COL Amy M. Tsuchida, MC

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** Sum P. Lee, M.D., Ph.D; MAJ Kazunori Yamamoto, MC; COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF; Scott J. Schulte, M.D.; Beth W. Alderman, M.D., MPH; Dr. Gerard Schellenberg, M.D.; Edward J. Boyko, M.D., Ph.D.; Gail Jarvik, M.D.; Katherine H. Moore, Ph.D.; MAJ Janice C. Stracener, MC; COL Dawn E. Light, MC

**Keywords:** Gallbladder, sludge, pregnancy

**Start Date:**

9/20/1996

**Est. Completion Date:**

Sep 02

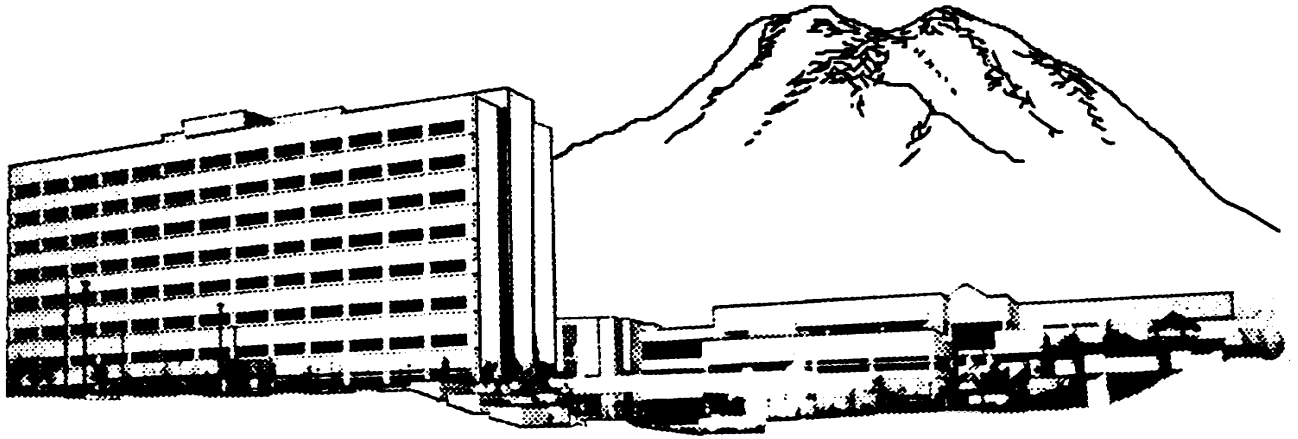
**Periodic Review:**

9/26/2000

**Study Objective:** The primary objective of this NIH-funded study is to determine the incidence of gallstones and sludge during pregnancy. Other objectives are to: 1) identify behavioral and genetic risk factors for the development and regression of sludge and stones; 2) elucidate the mechanism by such risk factors may induce gallstones; and 3) predict the development and regression of sludge and stones.

**Technical Approach:** This cohort study will include serial ultrasound tests of the gallbladder during pregnancy and post-partum. All women presenting for prenatal care will be eligible unless they: (1) do not speak English; (2) have had gallbladder surgery; (3) are over 20 weeks pregnant; (4) do not expect to deliver at MAMC; and (5) are less than 18 years of age. Eligible women who agree to participate will complete Participation and Consent Forms and under waist and hip circumference measurements. the ultrasonographers will test participants for evidence of sludge and stones at 10, 18, and 28 weeks of gestation and 6 weeks postpartum. For each ultrasound test, the study radiologist will review selected ultrasound images saved by the ultrasonographer. Participants who have stones or sludge at 6 weeks postpartum will return in 12 year for a follow-up ultrasound. At her time of each ultrasound, participants will be asked to complete a one-hour questionnaire and interview. They will also be asked to give an extra fasting blood sample at 128 weeks of gestation. Medical data from the CIS and CHCS will be downloaded and linked to study data.

**Progress:** This study has been reported as completed, Dec 01, with 4903 MAMC patients enrolled. An estimated 4800 completed the study with only 7 patients requesting to be dropped from the study with no reasons given. No patients were withdrawn and there were no adverse events reported. Final results are unavailable at this time. One article on preliminary enrollment had been published: Apolipoprotein E Genotype and the Risk of Gallbladder Disease in Pregnancy. Hepatology 31(1): 18-23,2000.



## **Detail Summary Sheets**

### **Geriatrics Service, Department of Medicine**

### Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 201/021 **Status:** Ongoing

**Title:** Reading Level, Cognitive Test, and Functional Task Performance in Cognitively Intact Elders

**Principal Investigator:** Ann L. Hightower, M.D.

**Department:** Medicine/Geriatrics

**Facility:** MAMC

**Associate Investigator(s):** None.

**Keywords:** reading testing, memory testing, geriatrics

**Start Date:**

11/28/2000

**Est. Completion Date:**

Oct 02

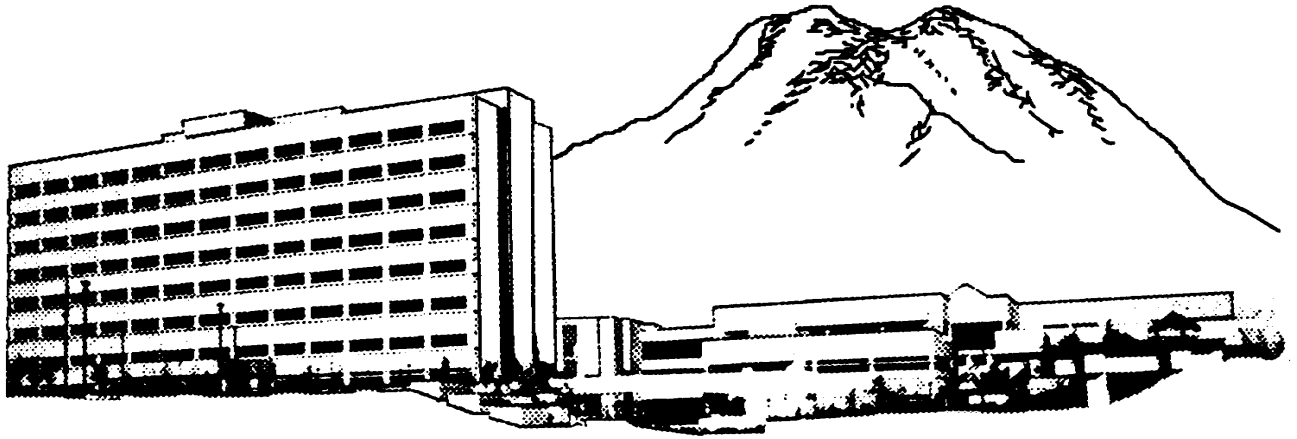
**Periodic Review:**

11/4/2002

**Study Objective:** The primary objective of the proposed study is to characterize the relationship between education (using reading level as a proxy), cognition and function in cognitively intact elders. The objectives have been divided into the following: Specific Aim I: (1) To determine if reading level is correlated with cognitive test performance in African American and White elders, (2) to describe the relationship between reading level and cognitive test performance across a range of reading levels, (3) to determine if there is a main effect for race in the correlation between reading score and cognitive test performance, (4) to determine if ethnic differences in cognitive test performance exist at a given reading level. Specific Aim II: (1) To determine if there is a correlation between reading level and performance on a structured independent activity of daily living functional task, the Medication Management Test (Gurland, et al, 1994). (This test provides information about cognitive ability as it relates to an important functional task; the ability to manage one's own medications)

**Technical Approach:** Instruments used to measure cognition and function in this study include the following: Mini-Mental State Exam (MMSE), Blessed Memory Information and Concentration Test (BMICT, which is part of the Blessed Dementia Rating Scale), Mini-Cog, Wide-Range Achievement Test-3 (WRAT-3), Geriatric Depression Scale (short-version), Boston Naming Test, Paragraph Recall (also known as Logical Memory, a subtest of the Wechsler Memory Scale), Category Naming Test, Trails A and B Test and the Medication Management Test. Because this is a correlative study, I will not be using or reporting standard scores but will be using raw scores.

**Progress:** The study has enrolled to date a total of 63 elders in the study, 21 of which are Madigan patients. Annual review was approved Jan 01. Since then, 1 additional Madigan patient enrolled. Goal for recruitment is 108 participants. No adverse events to report this reporting period. Study approval was renewed by University of Washington October 16, 2002 for the upcoming year. Some modifications that have been made in the study are: Change in years of education for participants from 8-15 to 8-16 to facilitate recruitment. Also the VA Research & Development office here required a new faculty project mentor be appointed since Dr Sanjay Asthana -the original UW/VA faculty mentor moved to the University of Wisconsin. Dr. Edward Boyko who is in the Dept of Medicine at the VA and is the fellowship program director agreed to be faculty mentor. His name is added to the list of co-investigators. In the process of awaiting UW Human Subjects Division review of a request to add Group Health as another study site, as they have a large registry of patients and have indicated they will allow me to recruit from a group of patients who are participants in a large longitudinal study of cognition. Group Health Research Committee has approved pending UW's approval. At this point, it is anticipated that the majority of further enrollees may not be Madigan patients.



## **Detail Summary Sheets**

### **Hematology/Oncology Service, Department of Medicine**

### Detail Summary Sheet

|                        |                        |                          |
|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/114 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** A Double-Blind Clinical Study to Compare Single IV Doses of Palonosetron, 0.25 mg or 0.75 mg, and Dolasetron 100 mg IV, in the Prevention of Moderately Emetogenic Chemotherapy-Induced Nausea and Vomiting, Protocol No. PALO-99-04

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

**Keywords:** Chemotherapy-Induced Nausea and Vomiting (CINV); moderately emetogenic chemotherapy; 5-HT<sub>3</sub> receptor antagonists; dolasetron

**Start Date:**  
6/26/2001

**Est. Completion Date:**  
Dec 02

**Periodic Review:**

**Study Objective:** To compare the efficacy of single IV doses of palonosetron 0.25 mg or 0.75 mg to dolasetron 100 mg IV in preventing moderately emetogenic chemotherapy induced nausea and vomiting. Secondary: To evaluate the safety and tolerability of palonosetron and its relative safety in comparison with dolasetron and to evaluate the effect of anti-emetic control with palonosetron or dolasetron on the quality of life of patients receiving moderately emetogenic chemotherapy.

**Technical Approach:** This clinical trial is a multicenter, Phase III, randomized, balanced, controlled, double-blind, parallel, stratified, and active comparator study of a new long acting antiemetic 5-HT<sub>3</sub> receptor antagonist medication with a currently available and approved antiemetic treatment for prevention of nausea and vomiting in patients receiving moderately emetogenic chemotherapy. At MAMC there are expected to be 10 to 20 patients enrolled to the PALO-99-04 protocol during approximately one year. Eligible patients must be 18 years or older, and able to provide written informed consent. Subjects at this clinical trial site will be identified from the Hematology/Oncology Clinic male and female patient population with histologically or cytologically confirmed malignant diseases, and who are scheduled on Day 1 of this study to receive a single dose of at least one of several protocol-listed moderately emetogenic chemotherapy agents as their major chemotherapeutic agent. A subgroup of enrolled patients in the PALO 04 and -05 trials (16-17% of the total randomized) will be randomized to receive and consented for a period of continuous ECG recording by Holter Monitor as part of the safety evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location. A separate consent form will be utilized for patients randomized to the Holter monitoring subgroup for each of these studies. Efficacy data and quality of life data for the periods between clinic/study visits will be collected using the tools of 1) a 5-day Patient Diary to record emetic episodes, rescue medication, severity of nausea, and evaluate patient satisfaction with antiemetic therapy, and 2) the Functional Living Index-Emesis Patient Questionnaire which will be completed twice during the study. General Procedures: Day 1, randomized patients will receive a single IV dose of 0.25 mg or 0.75 mg of palonosetron OR of dolasetron 100mg at 30 minutes prior to start of scheduled chemotherapy. For patients receiving Holter ECG monitoring, a 12 lead ECG will be performed 15 minutes after study drug is given, and single blood draw for PK analysis will be performed on selected study days. Patients return for follow up to the clinic at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will make telephone contact with the patient for follow up data.

**Progress:** Investigators reported this protocol closed at MAMC, effective 16 Apr 02. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

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|--|--|--|--|--------------------------|--|
| <b>Date:</b> 30 Sep 02   |  | <b>Number:</b> 201/115                 |  | <b>Status:</b> Completed |  |
| <b>Title:</b> A Double-Blind Clinical Study to Compare Single IV Doses of Palonosetron, 0.25 mg or 0.75 mg, and Ondansetron, 32 mg IV, in the Prevention of Highly Emetogenic Chemotherapy-Induced Nausea and Vomiting, Protocol No. PALO-99-05  |  |  |  |                          |  |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC   |  |  |  |                          |  |
| <b>Department:</b> Medicine/Hematology & Oncology  |  |  |  | <b>Facility:</b> MAMC    |  |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC   |  |  |  |                          |  |
| <b>Keywords:</b> Chemotherapy-Induced Nausea and Vomiting (CINV); highly emetogenic chemotherapy; 5-HT3 receptor antagonists; ondansetron;   |  |  |  |                          |  |
| <b>Start Date:</b><br>6/26/2001  |  | <b>Est. Completion Date:</b><br>Dec 02 |  | <b>Periodic Review:</b>  |  |
| <b>Study Objective:</b> Primary: To compare the efficacy of single IV doses of palonosetron 0.25 mg or 0.75 mg to ondansetron 32 mg IV in preventing nausea and vomiting induced by highly emetogenic chemotherapy. Secondary: To evaluate the safety and tolerability of palonosetron and its relative safety in comparison with ondansetron and to evaluate the effect of anti-emetic control with palonosetron or ondansetron on the quality of life of patients receiving moderately emetogenic chemotherapy.  |  |  |  |                          |  |
| <b>Technical Approach:</b> This clinical trial is a multicenter, Phase III, randomized, balanced, controlled, double-blind, double-dummy, parallel, stratified, and active comparator study of a new long acting antiemetic 5-HT3 receptor antagonist medication with a currently available and approved antiemetic treatment for prevention of nausea and vomiting in patients receiving highly emetogenic chemotherapy. Approximately 65 sites will participate in this study and the number of patients to be included in this study is estimated to be 669, distributed in 3 treatment arms of 223 men and women. At MAMC there are expected to be 2 to 5 patients enrolled to this protocol during approximately one year. Eligible patients must be 18 years or older, and able to provide written informed consent. Subjects at this clinical trial site will be identified from the MAMC Hematology/Oncology Clinic male and female patient population with histologically or cytologically confirmed malignant diseases, and who are scheduled on Day 1 of this study to receive a single dose of at least one of five protocol-listed highly emetogenic chemotherapy agents as their major chemotherapeutic agent.   |  |  |  |                          |  |
| 12-lead ECG testing is indicated by the protocol for patients at screening, at study drug treatment (for patients randomized to Holter ECG monitoring), at study day 2 and study day 8. The investigator is asked to review the ECG on site, and original ECG strips will be further evaluated by a cardiologist at a central location. A subgroup of enrolled patients in the PALO 04 and -05 trials (16-17% of the total randomized) will be randomized to receive and consented for a period of continuous ECG recording by Holter Monitor as part of the safety evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location. A separate consent form will be utilized for patients randomized to the Holter monitoring subgroup for each of these studies. Efficacy data and quality of life data for the periods between clinic/study visits will be collected using the tools of 1) a 5-day Patient Diary to record emetic episodes, rescue medication, severity of nausea, and evaluate patient satisfaction with antiemetic therapy, and 2) the FLIE (Functional Living Index-Emesis) Patient Questionnaire which will be completed twice during the study. |  |  |  |                          |  |
| General Procedures: On Study Day 1, randomized patients will receive a single IV dose of 0.25 mg OR 0.75 mg of palonosetron OR of ondansetron 32mg at 30 minutes prior to start of scheduled   |  |  |  |                          |  |

chemotherapy. In double-dummy blinded fashion, a 5ml IV bolus and a 50ml IV infusion will both be administered. At the investigator's discretion, and if so determined at the time of randomization, a single dose of dexamethasone or appropriate substitute medication may be given at 15 minutes before chemotherapy is started. For patients receiving Holter monitoring, a 12 lead ECG will be performed 15 minutes after study drug is given, and single blood draw for PK analysis will be performed on selected study days. Patients return at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will make telephone contact with the patient for follow up data. All patients have the option of continuing in the study after day 15 by enrolling to an open-label extension protocol that permits them to receive the study drug with up to 9 more cycles of chemotherapy if other inclusion and exclusion criteria continue to be met. Please refer to protocol submission for PALO-99-06. These patients return to the clinic for a 5th visit day 21-28.

**Progress:** Investigators reported this protocol closed at MAMC, effective 16 Apr 02. No patients enrolled in this study at MAMC.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 201/116

**Status:** Completed

**Title:** A Multicenter, Open-Label Study to Assess the Safety and Efficacy of IV Palonosetron for the Prevention of Chemotherapy-Induced Nausea and Vomiting in Repeated Chemotherapy Cycles, Protocol No. PALO-99-06

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

**Keywords:** Chemotherapy-Induced Nausea and Vomiting (CINV); moderately emetogenic chemotherapy; highly emetogenic chemotherapy; 5-HT<sub>3</sub> receptor antagonists

**Start Date:**  
6/26/2001

**Est. Completion Date:**  
Dec 02

**Periodic Review:**

**Study Objective:** To assess the safety of single dose IV palonosetron used in up to a maximum of 10 consecutive chemotherapy cycles, to assess the safety of single dose IV palonosetron plus dexamethasone used in a maximum of 10 consecutive chemotherapy cycles and to assess continued efficacy of palonosetron and palonosetron plus dexamethasone in repeated cycles of chemotherapy.

**Technical Approach:** This clinical trial is a multicenter, Phase III, uncontrolled, open-label, repeat-cycle safety study designed to assess the safety and efficacy of single IV doses of Palonosetron, 0.75mg, in the prevention of CINV in repeated chemotherapy cycles. Palonosetron is a new long acting antiemetic 5-HT<sub>3</sub> receptor antagonist medication. PALO-99-06 is an extension study to PALO-99-04 and PALO-99-05. Approximately 65 sites will participate in this study. At MAMC there are expected to be a maximum of 12 to 25 patients enrolled to the PALO-99-06 protocol. Enrollment in PALO-99-06 will remain open and patients will be allowed to continue in the protocol until at least 1200 additional chemotherapy cycles have been evaluated, and for as long as enrollment is ongoing in the PALO-99-04 and PALO-99-05 protocols, up to a maximum of 1700 cycles. Screening/baseline procedures may be performed on the same day as Study Day 1 and chemotherapy administration if feasible. On Study Day 1 patients will receive a single IV dose of 0.25 mg palonosetron as a 5-mL IV bolus at 30 minutes prior to administration of the major chemotherapeutic agent. For those patients who participated in PALO-99-05, a single dose of dexamethasone, 20mg IV, may be administered 15 minutes prior to chemotherapy. Dexamethasone will not be administered to PALO-99-06 patients who previously participated in PALO-99-04. Patients return to the clinic at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will contact patients by telephone for follow up data and progress. Patients who did NOT receive Holter ECG Monitoring in the PALO-04 and -05 trial they participated in have the option to take part during this study in evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Patients in this extension study may elect Holter participation for one of their PALO-99-06 plus chemotherapy treatment cycles. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location.

Patient Visit Procedures through Study Day 15 will be performed in the same way for each repeat chemotherapy cycle up to 9 additional cycles. Efficacy data collection will include a 5-day Patient Diary to record emetic episodes, rescue medication, and severity of nausea on study days 1 to 5.

**Progress:** Investigators reported this protocol closed at MAMC, effective 16 Apr 02. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/025 | <b>Status:</b> Ongoing |
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**Title:** A Multicenter, Phase III Randomized Trial for Stage IIIB or IV NSCLC Comparing Weekly Taxol (Paclitaxel) and Carboplatin (Paraplatin) Regimen Versus Standard Taxol and Carboplatin Administered Every Three Weeks, Followed by Weekly Taxol (TAX/MEN.12)

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** non-small cell lung cancer, taxol, carboplatin, NSCLC

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**Start Date:**  
11/28/2000

**Est. Completion Date:**  
Feb 02

**Periodic Review:**  
11/27/2001

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**Study Objective:** The primary objective of this study is to determine the overall patient survival rate for each of the two treatment regimens outlined in this study. The secondary objectives are to determine the time to disease progression for each regimen, to determine the objective response rate of the two treatment regimens, and to evaluate the safety and toxicity of the treatment regimens.

**Technical Approach:** This is a Phase III, multicenter, randomized, open-label trial to further investigate the safety and efficacy of weekly 1-hour infusions of paclitaxel (Taxol) and carboplatin for stages IIIB and IV NSCLC compared with a 3-hour infusion of the standard Taxol and carboplatin regimen administered every three weeks. During the induction phase, patients will be randomized to two treatment combination regimens of Taxol and carboplatin, followed by a maintenance phase that will consist of cycles of weekly Taxol for 3 weeks followed by a week of rest. Approximately 60 sites will participate in this study in the United States.

The primary efficacy endpoint will be the overall patient survival rate. The survival rate will be evaluated at 1,2,3,4, and 6 months and at 1 year for each of the dosing arms during the induction phase and for the maintenance phase. The secondary efficacy endpoints will be the objective response rate and the median time to disease progression. The response rate is defined as the percentage of patients that achieved a complete or partial response. The response rate for each treatment arm of the induction phase will be tested for equality to a 25% historical control rate. The time to progression will be evaluated during the induction phase and the maintenance phase. The time to progression data will be characterized by Kaplan-Meier curves and summarized using descriptive statistics

**Progress:** Four subjects have enrolled in this study at MAMC. MAMC serious adverse events were reported to the IRB in Nov. 01, Jan. 02 (2), and Feb. 02 for one subject, and in Nov. 01 for the other subject. Two patients have died due to disease progression. One continues in follow-up 14 months after enrolling to the study, and one is in follow-up after coming off study. One follow up event and one initial Non-MAMC adverse event in IND Safety reports were submitted for IRB notification in the previous year. One initial report is pending submission after discovery that it had been omitted from an April 2002 mailing to the site. A technical protocol deviation was reported and reviewed by the IRB in March 2002, with no patient safety issues found and no follow up action required. Subject recruitment remains open. Enrollment for this study is expected to be completed early in 2003.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/031                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Phase II Study of SGN-15 (cBR96-Doxorubicin Immunoconjugate) Combined with TAXOTERE® in Patients with Hormone Refractory Prostate Carcinoma, Protocol SG0001-015 |  |                         |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC   |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC   |  |                         |
| <b>Keywords:</b> prostate cancer, monoclonal antibody-drug conjugate, taxanes, anthracycline,  |  |                         |
| <b>Start Date:</b><br>1/22/2002  | <b>Est. Completion Date:</b><br>Feb 04 | <b>Periodic Review:</b> |

**Study Objective:** To evaluate the safety and efficacy of the investigational agent SGN-15 (cBR96-Doxorubicin immunoconjugate) administered in combination with weekly Taxotere®, and to compare the efficacy of SGN-15 administered in combination with weekly Taxotere® compared to weekly Taxotere® alone in patients with Hormone Refractory Prostate Cancer (HRPC).

**Technical Approach:** This study will be administered on an outpatient basis. Eligible patients will be identified from adult male patients receiving care in or referred to the Hematology and Oncology Clinic. These will be patients with histologically confirmed prostate cancer and either increasing dimensions of metastatic disease or increasing PSA level with documented metastatic disease while continuing androgen suppression. LewisY (Ley) antigen expression must be documented (on archived tumor specimen by histochemistry). Kits will be provided to the Pathology for LewisY testing when this evaluation is not already documented. Screening activities will include completion of informed consent, medical history including ECOG performance status and demographics, hematology and serum chemistries, serum testosterone level, imaging studies, and left ventricular function evaluation by MUGA or ECHO studies. Limitations to subject eligibility are placed on prior therapies received and coexisting disease and conditions. The screening evaluations will be completed within intervals of 3 days to 4 weeks prior to first study infusion. Patients will be assigned an identification number for study records, and eligible patients will be randomized in a 1:1 ratio to one of the two open-label treatment groups. Treatment group A will be treated with two drugs, SGN-15 and TAXOTERE™. SGN-15 will be given as a two-hour infusion once weekly for six weeks, followed by a two week rest period (Treatment visits will be once weekly on study Days 1, 8, 15, 22, 29, and 36). At the same treatment visits and following the SGN-15 infusion, TAXOTERE™ in standard dosage will be given as a 30-minute infusion. Treatment group B will be treated with TAXOTERE™ as a single agent in a 30-minute infusion once a week for six weeks followed by a two-week rest period. Patients will receive pre- and postmedication with steroid and antiemetic drugs. The doses of both chemotherapy drugs will be adjusted according to the side effects observed in the previous treatment. Routine clinical assessments of hematology, serum chemistries, PSA levels, and additional laboratory testing as clinically indicated, vital signs and physical examinations will be performed for safety monitoring. Follow up assessments also include adverse event reporting and quality of life assessment. Tumor response will be assessed after every treatment course by imaging techniques, physical exam, and changes in PSA and quality of life assessments. Patients who evidence stable disease, minimal, partial, or complete response and who have no evidence of progressive disease or significant toxicity may continue study therapy for up to a total of 6 courses.

**Progress:** MAMC IRB approved the protocol, Jan 02, and CIRO, Mar 02. Two subjects were randomized, one has received two cycles of study therapy and the other four cycles of study therapy. An amended Investigators' Brochure was issued and submitted for IRB notification, May 02. Three non-MAMC SAEs have been reported. No changes to the protocol or consent form have been made during this FY. Screening and enrollment remains ongoing.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/032 | <b>Status:</b> Ongoing |
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**Title:** A Phase II Study Using SGN-15 (cBR96-Doxorubicin Immunoconjugate) in Combination with TAXOTERE® for the Treatment of Advanced Stage or Recurrent Non-Small Cell Lung Carcinoma, Protocol SG0002-015

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** lung carcinoma, monoclonal antibody-drug conjugate, taxanes, anthracycline

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**Start Date:**

1/22/2002

**Est. Completion Date:**

Feb 04

**Periodic Review:**

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**Study Objective:** To evaluate the efficacy and the toxicity and safety profiles of the investigational agent SGN-15 (cBR96-Doxorubicin immunoconjugate) administered in combination with weekly Taxotere®, in patients with advanced stage or recurrent non-small cell lung carcinoma.

**Technical Approach:** This study will be administered on an outpatient basis. Eligible patients will be identified from adult patients receiving care in or referred to the Hematology and Oncology Clinic. These will be men and women with pathologically confirmed non-small cell lung cancer who have failed at least one but no more than two prior therapies for metastatic disease or who have a recurrence within 6 months of completing adjuvant chemotherapy. LewisY antigen expression must be documented and may be performed on archived or new biopsy tumor specimen by histochemistry. Screening activities will include completion of informed consent, medical history including ECOG performance status and demographics, hematology, serum Hcg (as indicated) and serum chemistries, imaging studies such as chest CT, tumor staging, and left ventricular function evaluation by MUGA or ECHO studies. The screening evaluations will be completed within intervals of 3 days to 4 weeks prior to first study infusion. Eligible patients will be randomized to the open label treatments in a 2:1 ratio in favor of the SGN-15 plus Taxotere® group. Treatment Arm A will be treated with two drugs, SGN-15 and Taxotere®. SGN-15 will be given as a two-hour infusion once weekly for six weeks, followed by a two week rest period (Treatment visits will be once weekly on study Days 1, 8, 15, 22, 29, and 36). At the same treatment visits and following the SGN-15 infusion, Taxotere® in standard dosage will be given as a 30-minute infusion. Treatment Arm B will be treated with Taxotere® as a single agent in a 30-minute infusion once a week for six weeks followed by a two-week rest period. Patients will receive pre- and postmedication with steroid, H2 blocker and antiemetic drugs selected by the investigator. The doses of both chemotherapy drugs will be adjusted according to the side effects observed in the previous treatment. Routine clinical assessments of hematology, serum chemistries, and additional laboratory testing as clinically indicated, vital signs and physical examinations will be performed for safety monitoring. Assessments also include adverse event reporting and quality of life assessment using the FACT-Taxane and FACT-L Questionnaires. Tumor response will be assessed after every treatment course by imaging techniques for tumor staging using the RECIST criteria. Patients who evidence stable disease, minimal, partial, or complete response and who have no evidence of progressive disease or significant toxicity may continue study therapy for up to a total of 6 courses. Patients will have a follow-up evaluation 6-8 weeks after therapy is discontinued.

**Progress:** MAMC IRB approved the protocol, Jan 02, and CIRO, Mar 02. An amended Investigators' Brochure was issued and submitted for IRB notification, May 02. Three non-MAMC SAEs have been reported. One subject enrolled and has completed 2 courses of therapy. Protocol Amendment #1 and revised consent form were approved by MAMC IRB, Aug 02.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/114                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Phase III, Multicenter, Randomized, Active-controlled Clinical Trial to Evaluate the Efficacy and Safety of rhuMAb-VEGF (BEVACIZUMAB) in Combination with Standard Chemotherapy in Subjects with Metastatic Colorectal Cancer (AVF2107g)  |  |                                      |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC  |  |                                      |
| <b>Keywords:</b> metastatic colorectal cancer, monoclonal antibody, rhuMab-VEGF, BEVACIZUMAB, chemotherapy, 5-FU, leucovorin  |  |                                      |
| <b>Start Date:</b><br>7/25/2000   | <b>Est. Completion Date:</b><br>Sep 04 | <b>Periodic Review:</b><br>7/23/2002 |
| <b>Study Objective:</b> To evaluate the efficacy of multiple administrations of rhuMAb-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer, as measured by duration of survival and to evaluate the safety of multiple administrations of rhuMAb-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer.   |  |                                      |
| <b>Technical Approach:</b> rhuMab-VEGF (Bevacizumab) is an experimental, humanized monoclonal antibody using recombinant DNA technology, directed against vascular endothelial growth factor, or VEGF. Following a 28 day screening period, eligible subjects will be randomized into one of three treatment arms, (1) 5-FU/leucovorin/CPT-11 plus placebo, (2) 5-FU/leucovorin/CPT-11 plus study drug, or (3) 5-FU/leucovorin plus study drug. The treatment period will last approximately 23 months with a 14 day follow-up. Subjects will be asked to periodically complete Quality of Life Questionnaires and blood samples will be sent to an outside lab for pharmacokinetic testing. Second-line treatment options will be offered under this protocol if there is disease progression, depending on the treatment arm originally assigned. Subjects will be removed from the study if the disease progresses further following second-line treatment. A safety analysis will be conducted after the first 50 patients treated with the study drug and CPT-11. At the conclusion of the study, if the tumor is stable or smaller and if subjects received rhuMab-VEGF, they may be eligible to continue to receive the study drug under an extension study. |  |                                      |
| <b>Progress:</b> This protocol closed to enrollment, Apr 02, but underwent annual continuation review and received approval to continue, May 02, for subject follow up activities. The IRB requested and was provided supplemental safety information obtained from the study sponsor Medical Monitor from a recent independent Interim Safety Analysis. One subject was withdrawn from the study due to a serious adverse event, Mar 02. Two Subjects died due to disease progression. One subject with disease progression continues in follow up, but is no longer receiving study therapy. Protocol Amendments 1, 2, 3 were submitted and approved in March, August, and October 2002. The consent form was revised with updated safety information in January and March 2002 and by using a consent addendum twice (July and September 2002) to notify of new non-MAMC safety information. All data collection has been returned and reviewed. The site is expected to close all study activities early in FY 2003.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/083 | <b>Status:</b> Ongoing |
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**Title:** A Randomized Phase III Trial of Gemzar versus Doxil with Crossover Treatment Option for Patients with Platinum-Refractory Ovarian, Fallopian Tube or Primary Peritoneal Cancer Undergoing Second or Third-Line Chemotherapy, Protocol Number: B9E-US-S301

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC; LCDR John D. O'Boyle, MC, USN

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**Keywords:** ovarian cancer, Fallopian tube, primary peritoneal cancer, platinum-refractory cancer, Doxil, Gemzar

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**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Jul 05

**Periodic Review:**

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**Study Objective:** Primary Objectives: To compare progression free survival in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy who are treated with Doxil or Gemzar. Secondary Objectives: To compare response rate, duration of response, time to treatment failure, survival, and quality of life in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy who are treated with Doxil or Gemzar.

**Technical Approach:** At MAMC there are expected to be 5-10 patients enrolled during approximately one year. Patient screening will include written informed consent, medical history and demographics, tumor assessment by exam or imaging, FACT-O questionnaire, Zubrod Performance Status, LVEF, chemistry and hematology, CA-125 tumor marker, contraceptive status and serum pregnancy test. Patients on the Doxil arm will be treated with 50 mg/m<sup>2</sup> on Day 1 of each 28 day cycle. Treatment will continue for two cycles after a complete response, or until a cumulative maximum dose of 500 mg/m<sup>2</sup> has been given. Patients on the Gemzar arm will be treated with 1000mg/m<sup>2</sup> on Days 1 and 8 of a 21 day cycle. Treatment will continue for up to two cycles after complete response is attained. For patients with stable disease there is no maximum number of Gemzar cycles. Patients who have progressive disease may cross over to the other treatment arm if they are eligible. Patients will be monitored every cycle for toxicities, chemistry, hematology, performance status and CA-125 tumor staging. Dose adjustments will be made based on NCI toxicity criteria. FACT-O Quality of Life questionnaire will be administered every other cycle, and tumor assessment imaging will be performed every 12 weeks. Primary efficacy will be evaluated using Kaplan-Meier techniques. Secondary efficacy analysis will be conducted on response rate, duration of response, time to treatment failure, survival and quality of life. Response rates from the two treatment arms will be compared using Fisher's Exact test. Summaries on toxicity parameters will be provided.

**Progress:** This study has not yet been initiated at MAMC. The protocol received IRB approval in June 2002 and CIRO approval in August 2002. An agreement between the study sponsor and the Henry M. Jackson Foundation for study support is still pending.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/114                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> CTSU/CALGB 40101: Cyclophosphamide and Doxorubicin (CA) (4 vs. 6 Cycles) versus Paclitaxel (12 Weeks vs 18 Weeks) as Adjuvant Therapy for Women with Node-Negative Breast Cancer: a 2X2 Factorial Phase III Randomized Study   |  |                         |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC   |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC   |  |                         |
| <b>Keywords:</b> Node-Negative Breast Cancer   |  |                         |
| <b>Start Date:</b><br>9/24/2002  | <b>Est. Completion Date:</b><br>Oct 05 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> To determine the equivalence of weekly paclitaxel with CA as adjuvant therapy for women and to determine if longer therapy is superior to shorter of either CA or paclitaxel.To determine the equivalence of weekly paclitaxel with CA and the potential superiority of longer vs. shorter therapy in relation to overall survival, lical control (regardless of metastatic status) and time to distant matastases (regardless of recurrence status)To compare toxicities of shor and long course CA and paclitaxel as adjuvant therapy.To determine the effect of long and short course CA and paclitaxel on the induction of menopause for pre-mentalpausal. |  |                         |
| <b>Technical Approach:</b> Comparing standard treatment (CA (4 cycles vs 6 cycles) and Taxol (12 weeks versus 18 weeks) for node-negative breast cancer. XRT and aromatase inhibitor or tamoxifen are optional after chemo.  |  |                         |
| <b>Progress:</b> This study recently received IRB approval and has not yet been initiated at MAMC.   |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/089 | <b>Status:</b> Ongoing |
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**Title:** CTSU/CALGB 49907: A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or High-Risk Node Negative Breast Cancer

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** Node negative breast cancer

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**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Jul 05

**Periodic Review:**

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**Study Objective:** To compare the effectiveness of standard chemotherapy (CMF or AC) with single agent capecitabine with respect to disease-free survival in women 65 years and older with local and regional breast cancer. To compare the effectiveness of standard chemotherapy regimens with capecitabine with respect to overall survival. To determine the effects of each treatment regimen on quality of life and physical function. To assess the toxicity of each treatment program. To study the adherence to an oral chemotherapy regimen in older patients.

**Technical Approach:** This study compares the oral anti-cancer drug capecitabine to standard adjuvant therapy of either Cyclophosphamide, Methotrexate and Fluorouracil or Doxorubicin and Cyclophosphamide in women who have complete breast cancer surgery and are over 65 years old. The study will attempt to find a survival her forth difference in relapse rates or a quality of life.

**Progress:** This protocol has not yet been initiated at MAMC.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/087                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> CTSU/CALGB 9633: A Phase III Study of Adjuvant Chemotherapy After Resection for Patients With T2N0 Stage I Non-Small Cell Carcinoma of the Lung |  |                         |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC  |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC  |  |                         |
| <b>Keywords:</b> Stage I Non-Small Cell Carcinoma   |  |                         |
| <b>Start Date:</b><br>6/25/2002   | <b>Est. Completion Date:</b><br>Jul 05 | <b>Periodic Review:</b> |

**Study Objective:** To determine if adjuvant chemotherapy can favorably alter the prognosis of the subgroup of resected Stage I patients who, following complete surgical resection, are defined as "high risk" based on the presence of a T2N0. To compare failure-free survival of patients with T2N0 Stage I NSCLC who have or have not been treated with adjuvant chemo. To determine the toxicities associated with adjuvant chemotherapy. To describe the pattern of disease recurrence.

**Technical Approach:** The standard therapy after surgical resection of early stage lung cancer is observation. This study compare observation to adjuvant chemotherapy to see if there is any difference in relapse rates or survival

**Progress:** This study has not received final approval and has not yet been initiated at MAMC.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/088 | <b>Status:</b> Ongoing |
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**Title:** CTSU/E1A00: A Randomized Phase III Trial of Thalidomide (NSC #66847) Plus Dexamethasone versus Dexamethasone in Newly Diagnosed Multiple Myeloma

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

**Keywords:** Myeloma, thalidomide, dexamethasone

**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Jul 05

**Periodic Review:**

**Study Objective:** To evaluate the response rate and toxicity of thalidomide plus dexamthasone and dexamethasone alone in patients with newly diagnosed myeloma. To study the effect of thalidomide on bone marrow microvessel density and angiogenesis grade and on the expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in the marrow.

**Technical Approach:** Compare a standard treatment for myeloma, dexamethasone to dexamethasone plus thalidomide. The goal of the study is to see if there is any difference between the two with respect to response rate, complications and quality of life or survival.

**Progress:** One patient was enrolled to this protocol during FY02. No SAEs were reported. Patient enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/029                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> CTSU/NSABP B-34: A Clinical Trial Comparing Adjuvant Clodronate Therapy vs Placebo in Early-Stage Breast Cancer Patients Receiving Systemic Chemotherapy and/or Tamoxifen or No Therapy   |  |                         |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC  |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC  |  |                         |
| <b>Keywords:</b> Clodronate placebo breast cancer   |  |                         |
| <b>Start Date:</b><br>1/22/2002   | <b>Est. Completion Date:</b><br>Feb 05 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> (1) This Phase III is to determine whether clodronate administered for 3 years either alone or in addition to adjuvant chemotherapy and/or hormonal therapy, in patients with early-stage breast cancer will improve disease-free survival, (2) to determine whether clodronate will: reduce the incidence of skeleton metastases, improve overall survival, improve relapse-free survival, reduce the incidence of non-skeleton metastases, reduce the incidence of skeletal morbidity (skeletal fractures, hypercalcemia, skeletal pain, need for radiation therapy, spinal cord compression) and (3) to investigate the relevance of serum markers of bone turnover as a prognostic factor for the development of bone metastasis. |  |                         |
| <b>Technical Approach:</b> After patients diagnosed with early stage breast cancer are given chemotherapy, they will be randomized to take either clodronate or placebo daily for three years. Patients will be followed for 5 years.   |  |                         |
| <b>Progress:</b> This study has not received final approval and has not yet been initiated at MAMC.   |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/043 | <b>Status:</b> Ongoing |
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**Title:** CTSU/RTOG 98-04: Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk Duct Carcinoma In-Situ (DCIS) of the Female Breast

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** tamoxifen radiation therapy carcinoma DCIS breast

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**Start Date:**  
2/26/2002

**Est. Completion Date:**  
Feb 05

**Periodic Review:**

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**Study Objective:** (1) Comparing whole breast radiation +/- tamoxifen compared to wide excision to negative margins alone +/- tamoxifen, in decreasing or delaying the appearance of local failure, both invasive and in situ, and preventing need for mastectomy, (2) assess distant disease free survival patients in either arm who fail with progression can be successfully salvaged with further definitive local therapy and adjuvant systemic therapy, (3) setting up a working pathology classification system for DECIS, (4) establishing an epidemiological questionnaire registry for companion studies of biomarkers, and (5) establish tissue bank of patients who progress to local failure in study breast.

**Technical Approach:** To compare the efficacy of tamoxifen with or without whole breast radiation, in decreasing or delaying the appearance of local failure, both invasive and in-situ, and preventing the need for mastectomy in women with ductal carcinoma in-situ (DCIS) of the breast.

**Progress:** This study has not yet been initiated at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 99/093                  | <b>Status:</b> Terminated            |
| <b>Title:</b> Phase II Trial of Gemcitabine and Herceptin in HER2 Overexpressing Metastatic Breast Cancer |  |                                      |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC                |  |                                      |
| <b>Keywords:</b> Cancer:breast, Gemcitabine, Herceptin, HER2, overexpression                              |  |                                      |
| <b>Start Date:</b><br>8/24/1999   | <b>Est. Completion Date:</b><br>Jul 01 | <b>Periodic Review:</b><br>7/24/2001 |

**Study Objective:** 1) To determine the response rates of complete response, partial response, stable disease and progressive disease. 2) To document the median time to progression and median survival of disease. 3) To monitor toxicities of Grades 3 or higher to be reported (toxicities graded based on the NCI common toxicity grading scheme).

**Technical Approach:** This is a Phase II multicenter trial conducted in military medical centers experienced in the treatment of breast cancer. This study will investigate the utility of using serum Her-2/neu as a clinical marker of disease responses as well as disease progression in metastatic breast cancer patients receiving systemic therapy with overexpress Her-2/neu in their malignant tissue. The study will investigate the response rate, time to treatment failure, overall survival and toxicity/safety profile of a novel combination of Gemcitabine and Herceptin in patients with metastatic breast cancer. Both of the drugs will be administered weekly in patients whose breast cancer overexpresses the HER2 proto-oncogene.

**Progress:** Protocol terminated without having started. No patients ever enrolled.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/030 | <b>Status:</b> Ongoing |
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**Title:** Protocol UAB 9912 - A Phase II Study Using SGN-15 (cBR96-Doxorubicin Immunoconjugate) in Combination with Taxotere® for the Treatment of Metastatic or Recurrent Breast Carcinoma

**Principal Investigator:** MAJ David E. McCune, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** immunoconjugate, monoclonal antibody-drug conjugate, taxanes, anthracycline, breast carcinoma, cytotoxic therapies

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**Start Date:**  
1/22/2002

**Est. Completion Date:**  
Feb 03

**Periodic Review:**

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**Study Objective:** To evaluate the efficacy, toxicity and safety profile of the investigational agent SGN-15 (cBR96-Doxorubicin immunoconjugate) administered in combination with weekly Taxotere®, in patients with advanced stage or recurrent breast carcinoma (BC).

**Technical Approach:** This is an open-label, non-randomized trial. Patients will be assigned an identification number for study records. Each eligible patient registered will be treated with two drugs, SGN-15 and Taxotere®. SGN-15 will be given as a two-hour infusion once weekly for six weeks, followed by a two week rest period (Treatment visits will be once weekly on study Days 1, 8, 15, 22, 29, and 36). At the same treatment visits and following the SGN-15 infusion, Taxotere® in standard dosage will be given as a 30-minute infusion. Patients will receive pre- and postmedication with steroid (prevention of fluid retention and hypersensitivity reactions), H2 blocker and antiemetic drugs selected by the investigator. The doses of both chemotherapy drugs will be adjusted according to the side effects observed in the previous treatment. Routine clinical assessments of hematology, serum chemistries, , and additional laboratory testing as clinically indicated, vital signs and physical examinations will be performed for safety monitoring. Assessments also include adverse event reporting. Grading of toxicities will be by Modified NCI Common Toxicity Criteria. Tumor response will be assessed after every treatment course by imaging studies and/or tumor markers as appropriate. Patients who evidence stable disease, minimal, partial, or complete response and who have no evidence of progressive disease or significant toxicity may continue study therapy for up to a total of 6 courses. If at any time evaluations demonstrate disease progression, the patient will be withdrawn from the study. All supportive measures will be given throughout the study according to institution standards, including but not limited to additional antiemetic therapy and antibiotics at discretion of the investigators. Patients will have a follow-up evaluation within 4 weeks after therapy is discontinued.

**Progress:** MAMC IRB approved the protocol, Jan 02, and CIRO, Mar 02. One subject was randomized and has received two cycles of study therapy. An amended Investigators' Brochure was issued and submitted for IRB notification, May 02. Three non-MAMC SAEs have been reported. Amendment #8 to the protocol was approved by MAMC IRB, Jul 02, with administrative changes to the informed consent form due to a protocol name and number change due to transfer of the IND. The overall study closed to further enrollment, Oct 02.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/100                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Randomized Study of Dacarbazine versus Dacarbazine Plus G3139 (Bcl-2 Antisense Oligonucleotide) in Patients with Advanced Malignant Melanoma, Protocol GM301 |  |                         |
| <b>Principal Investigator:</b> MAJ David E. McCune, MC   |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC   |  |                         |
| <b>Keywords:</b> decarbazine, melanoma DTIC antisense bcl-2  |  |                         |
| <b>Start Date:</b><br>7/23/2002  | <b>Est. Completion Date:</b><br>Dec 03 | <b>Periodic Review:</b> |

**Study Objective:** To compare the survival of subjects with advanced malignant melanoma treated with dacarbazine (DTIC) alone versus dacarbazine combined with G3139 (Bcl-2 antisense oligonucleotide). To compare safety, progression free survival, response rate, and durable response rate between the two treatment groups.

**Technical Approach:** This pharmaceutical study is a Phase III, randomized, multicenter, open-label study to compare the survival, progression-free survival, response rate, durable response rate, and safety between treatment with Arm A (DTIC) and Arm B (DTIC + G3139) of patients with advanced malignant melanoma. At MAMC, the goal enrollment is 2 to 5 patients. Eligible patients for this study will be identified from patients receiving treatment in the Hem/Onc Clinic. Subjects need to be 18 years or older, must have advanced malignant melanoma, and be candidates for DTIC therapy. Patients may not have received prior cytotoxic chemotherapy regimens. Further screening will include completion of informed consent, medical history with ECOG performance status and demographics, hematology, chemistry and serum pregnancy test for women of childbearing potential, EKG, and tumor assessment by physical exam or imaging as appropriate. Patients will be randomized in a 1:1 ratio to treatment with DTIC (Arm A) or DTIC plus G3139 (Arm B). Patients on Arm A will be treated with DTIC IV on Day 1 of each 21-day cycle. Treatment will continue as tolerated, and if disease is stable or responding, for up to a total of 8 cycles. In Arm B, G3139 will be administered IV through a central line using an ambulatory infusion pump for 5 consecutive days starting on day 1 of a 21 day cycle. Continuous ambulatory infusion pumps will be supplied by Genta Incorporated for the duration of the study. DTIC will be administered IV on day 6 of the 21 day cycle immediately after the G3139 infusion is discontinued. Treatment will continue if tolerated until disease progression or for a total of 8 cycles. Patients enrolled in Arm B who achieve complete or partial response or stable disease at the end of 8 cycles may be eligible to continue treatment for an additional 6 months by enrolling in a separate open-label continuation protocol. Subjects will continue to be followed with physical exam, laboratory assessments, and imaging as appropriate every two months after treatment for survival. Study subjects will receive full supportive care during the study including antiemetics and appropriate antibiotic therapy per standard of care. Dose adjustments will be made based on NCI toxicity criteria. Tumor measurements by physical exam and/or scan will be performed every other cycle. The primary endpoint measure will be progression free survival. In treated patients, performance status, patient weight, and tumor-related symptoms will also be compared. First stage analysis will be based upon data generated from randomization to the appearance of progressive disease. Primary efficacy will be evaluated using Kaplan-Meier techniques.

**Progress:** The protocol was approved by MAMC IRB on 23 July 2002. All study supplies are on site. The study coordinator attended the Investigator's Meeting held in Chicago in August. Regulatory documentation issues by the contract research organization for the sponsor have delayed opening of the study to patients until recently. Screening for possible study enrollments is now open.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/107 | <b>Status:</b> Ongoing |
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**Title:** Randomized Study of Docetaxel Versus Docetaxel Plus Genasense™ (Bcl-2 Antisense Oligonucleotide) in Patients with Previously Treated Non-Small Cell Lung Cancer, No. GN304

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

**Keywords:** Non-Small Cell Lung Cancer, Docetaxel, Antisense, Bcl-2

**Start Date:**  
8/27/2002

**Est. Completion Date:**  
Sep 04

**Periodic Review:**

**Study Objective:** To compare the survival of subjects with advanced non-small cell lung cancer treated with docetaxel alone versus docetaxel combined with Genasense (Bcl-2 antisense oligonucleotide). To compare response, time to progression, tumor-related symptoms, and safety in the two treatment groups.

**Technical Approach:** The purpose of this study is to evaluate an investigative antisense agent (Genasense) shown in vitro and in clinical studies to down-regulate expression of Bcl-2 protein by cancer cells, a protein which may enable tumor resistance to cell death that is initiated by standard chemotherapies. In this advanced non-small cell lung cancer study antisense treatment will be given with Taxotere (docetaxel) and tumor response and safety will be compared to therapy with Taxotere alone. This study is a randomized, multicenter, open label, Phase III design clinical trial. The study was originally opened in other centers with an imbedded Phase II component in which an interim analysis for safety and response was conducted after 35 patients were enrolled into each of two arms of the study. Phase II results suggest superior antitumor efficacy on the antisense treatment arm and support further study of this regimen. This Phase III study will include a minimum of 280 patients randomized in a 1:1 ratio to docetaxel or docetaxel+Genasense. Approximately 35 centers will participate. Study endpoints include the primary efficacy variable of survival and secondary efficacy variables of response rate, proportion of patients surviving at 6 and 12 months, duration of response, time to disease progression and other measures of clinical benefit such as change in performance status. All patients in the study will be prospectively stratified by response to prior chemotherapy regimen, ECOG performance status and prior paclitaxel treatment.

**Progress:** This study recently received IRB approval and has not yet been initiated at MAMC.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/085                 | <b>Status:</b> Terminated           |
| <b>Title:</b> A Phase II Trial of Recombinant-Human Granulocyte-Macrophage Colony Stimulating Factor (rhu-GM-CSF, Leukine) in Chronic Diabetic and Venous Stasis Wounds |  |                                     |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                     |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; Vickie R. Driver, DPM; CPT Amy L. Young, DO  |  |                                     |
| <b>Keywords:</b> rhuGM-CSF, venous stasis, diabetes, wound healing  |  |                                     |
| <b>Start Date:</b><br>5/23/2000   | <b>Est. Completion Date:</b><br>Jan 02 | <b>Periodic Review:</b><br>5/9/2002 |

**Study Objective:** (1) Assess the efficacy of applying rhu-GM-CSF peri-lesionally to chronic diabetic and venous chronic wounds at a dose of 500mcg twice weekly to decrease time to wound healing and (2) Assess the safety, as an adjunct to standard wound care, of peri-lesional rhu-GM-CSF to improve time to wound healing.

**Technical Approach:** This study is an open, single-arm pilot study. 30 male/female eligible patients, over 18 years-old, with chronic wounds as a result of the verifiable diagnosis of diabetes or venous stasis will receive rhu-GM-CSF (Leukine) twice weekly through peri-lesional injection in a four-points-of-the-compass fashion of their wounds for a total of twenty weeks. Wound size will be measured at entry, at each visit, and at the conclusion of therapy. The change in the cross-sectional area of the wound will be recorded for each patient and reported as the primary endpoint of the study. Patients will be sequentially enrolled with interim analysis at twenty patients. The secondary endpoint of the study is the incidence of toxicity with the study drug. Toxicity will be assessed at every visit, and recorded according to the NCI Common Toxicity Criteria. Efficacy will be measured by comparison to historical records and safety monitored throughout the study. This data will be used to initiate a phase III trial to develop and utilize a topical gel formulation of rhu-GM-CSF.

**Progress:** This protocol was reported as terminated. The study sponsor, Immunex, did not allow this study to be initiated at MAMC.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/011 | <b>Status:</b> Completed |
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**Title:** A Prospective, Multicenter, Open-label Clinical Evaluation of the Effect of IV Zometa 4mg on Pain, Quality of Life, and Time in Infusion Chair in Breast Cancer, Multiple Myeloma, and Prostate Cancer Patients with Cancer-Related Bone Lesions. Protocol No. CZOL446EUS16

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC

**Keywords:** bisphosphates, osteoblast, bone mineralization, osteoclast, calcium resorption, bone metastasis

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| <b>Start Date:</b><br>10/23/2001 | <b>Est. Completion Date:</b><br>Sep 03 | <b>Periodic Review:</b> |
|----------------------------------|--|-------------------------|

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**Study Objective:** The overall objective of the clinical trial is to assess effects and tolerability of Zometa® (zoledronic acid) administered every 3-4 weeks in patients with bone metastases from breast cancer, multiple myeloma, or prostate cancer. Primary Objective is assessment of pain course over time measured by a 100mm Visual Analog Scale (VAS). Secondary Objectives include infusion time ("time in chair"), quality of life measures assessed by the Functional Assessment of Therapy Scale-General (FACT-G) questionnaire, and evaluation of the safety of Zometa® 4mg given every 3-4 weeks to cancer patients with bone metastases.

**Technical Approach:** This pharmaceutical clinical trial is a Phase IV, prospective, multicenter open-label single-group study to obtain additional data on patients' course of pain, quality of life, time in chair for infusion and safety while receiving treatment with Zometa®, a 3rd generation bisphosphonate of greater potency than earlier drugs of this type. Study patients will serve as his or her own control. To participate, patients must have multiple myeloma, breast cancer or prostate cancer with at least one bone lesion and treatment with a bisphosphonate must be indicated. ECOG performance status must be 0, 1, or 2. Approximately 500 patients from about 100 centers will be enrolled with 5-10 patients enrolled at MAMC during approximately two years. All eligible patients will be treated with up to 6 infusions of study drug at 3-4 week intervals. Safety assessments include laboratory tests, vital signs and physical exams. VAS, FACT-G, and time in infusion chair assessments will be performed during study visits. Antineoplastic therapies, radiation therapy, corticosteroid therapies, and other concomitant therapies are allowed if not expected to affect osteoclast activity. Data from all centers will be combined and summarized according to demographic and baseline characteristics, disease type, pain, time in chair, and quality of life and safety observations and measurements. Sample size is based on feasibility parameters rather than statistical considerations. Changes from baseline data will be evaluated using descriptive analysis, paired t-tests, and regression analysis.

**Progress:** Ten subjects enrolled in this study at MAMC and received study treatment. Seven completed all study treatments in Aug 02. Two subjects died due to disease progression during the active study period and 1 subject relocated out of the area and was subsequently withdrawn from the study. Amendment 2, of 4 Dec 01, and a revised consent form were approved by MAMC IRB in Feb 02. A revised investigator brochure version 8 was submitted and the informed consent administratively revised in May 02, after closing of enrollment to the trial. A CIRO audit was conducted of this study at MAMC, July 02. A consent form was identified that had been signed in pencil; this was corrected and reported to MAMC IRB in July 02. Six reports of non-MAMC SAEs were submitted to the IRB for review. This study has been permanently closed at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/082                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> CTSU E2100: A Randomized Phase III Trial of Paclitaxel versus Paclitaxel plus Bevacizumab (rhuMAb VEGF) as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer   |  |                         |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC   |  |                         |
| <b>Keywords:</b> Metastatic breast cancer   |  |                         |
| <b>Start Date:</b><br>6/25/2002   | <b>Est. Completion Date:</b><br>May 05 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> (1) To determine the time to treatment failure of patients with chemotherapy naïve metastatic breast cancer randomized to treatment with either Paclitaxel alone or Paclitaxel with Bevacizumab, (2) to compare the objective response rate, duration of response, and overall survival of Paclitaxel to that of the combination of Paclitaxel plus Bevacizumab, (3) to compare the toxicity of Paclitaxel to that of Paclitaxel in combination with Bevacizumab, (4) to compare the QOL of patients treated with Paclitaxel to that of the combination of Paclitaxel plus Bevacizumab as first-line therapy for metastatic breast cancer, (5) to compare the changes in surrogate markers of angiogenesis and response including VEGF and VCAM-1 expression during treatment with Paclitaxel to that of Paclitaxel plus Bevacizumab. |  |                         |
| <b>Technical Approach:</b> This study will compare the effect of Paclitaxel with and without the monoclonal antibody Bevacizumab on locally recurrence of metastatic breast changes, as well as measure surrogate markers of angiogenesis during treatment.   |  |                         |
| <b>Progress:</b> This study has not yet been initiated at MAMC, pending completion IRB approval process.  |  |                         |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 93/147      **Status:** Ongoing

**Title:** NSABP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Inez J. Sanchez-Rivera, MC

**Keywords:** cancer:rectum, 5-FU, leucovorin, radiotherapy

**Start Date:**  
8/6/1993

**Est. Completion Date:**  
Jul 98

**Periodic Review:**  
6/7/2002

**Study Objective:** 1). To determine whether the administration of chemotherapy (chemo) with radiotherapy (RTX) preoperatively is more effective than administration of chemo and RTX (C&R) postoperatively in improving disease-free survival and survival in patients with operable carcinoma of the rectum. 2). To determine if the administration of the above C&R preoperatively results in improvement local recurrence rates when compared with the regimen administered post-operatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative C&R and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative C&R on the tumor size and pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdomino-perineal resection and local excision alone.

**Technical Approach:** Patients with operable adenocarcinoma of the rectum will receive seven cycles of 5-FU (FU) + leucovorin (LV) and radiotherapy (RTX), where the first three cycles are given preoperatively and the remaining four postoperatively, to seven cycles of FU-LV and RTX given postoperatively. The patients will be randomized into 2 groups. Group 1 patients, in cycle 1, will receive LV 500 mg/m<sup>2</sup> by IV infusion and FU 500 mg/m<sup>2</sup> will be started 1 hr later. Treatment will be given weekly for 6 weeks followed by a rest period. Treatment will be restarted 21 days after the date of administration of the sixth dose of the previous cycle. RTX will begin after completion of cycle 1. FU 325 mg/m<sup>2</sup>/day and LV 20 mg/m<sup>2</sup>/day will be given for 5 days during the first and fifth weeks of RTX (cycles 2 and 3). Surgery will be performed after completion of radiation therapy. After recovery from surgery, four more cycles of FU with LV, as in cycle 1, will be given for a total of seven cycles. Groups 2 patients should have surgery performed no later than 3 weeks after randomization. Chemo will begin after recovery from surgery is complete but no later than 4 weeks postoperatively. LV and FU will be administered as in Group 1. RTX will begin after completion of cycle 1. Cycle 4 should begin after completion of RTX when counts allow, but no later than 5 weeks. Four more cycles of FU with LV will be given for a total of seven cycles.

**Progress:** This protocol closed to patient accrual, 27 Aug 99. One patient enrolled at MAMC and continued to be followed during FY02.

### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 83/056                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; LTC James E. Congdon, MC; COL Friedrich H. Stutz, MC; COL Irwin B. Dabe, MC; MAJ Timothy J. O'Rourke, MC; MAJ Alfred H. Chan, MC; MAJ Thomas M. Baker, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; Howard Davidson, M.D.  |  |                                      |
| <b>Keywords:</b> cancer:breast,surgery,biological parameters   |  |                                      |
| <b>Start Date:</b><br>3/18/1983  | <b>Est. Completion Date:</b><br>Feb 85 | <b>Periodic Review:</b><br>1/31/2002 |
| <b>Study Objective:</b> To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whos pathological size is >3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).   |  |                                      |
| <b>Technical Approach:</b> Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight. |  |                                      |
| <b>Progress:</b> Total of 12 patients were enrolled to protocol from Feb 83 to Sep 86. This study closed to patient entry 15 May 88. Seven patients remain on follow-up.   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/119 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy

**Principal Investigator:** MAJ Patrick Williams, MC

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|---|-----------------------|
| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Raymond S. Lance, MC; MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Kurt L. Hansberry, MC; CPT Timothy O. Taylor, MC; CPT Michael D. Bagg, MC; CPT Bradley F. Schwartz, MC; MAJ J. Brantley Thrasher, MC; LTC Luke M. Stapleton, MC; LTC Kenneth A. Bertram, MC; MAJ Patrick L. Gomez, MC

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**Keywords:** Cancer:prostate, radiotherapy

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**Start Date:**

6/3/1994

**Est. Completion Date:**

Jun 98

**Periodic Review:**

5/9/2002

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**Study Objective:** 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

**Technical Approach:** Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

**Progress:** This study closed to patient entry, 17 Jan 97. One patient enrolled at MAMC and continued to be followed during FY02.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 88/066

**Status:** Ongoing

**Title:** SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; COL Irwin B. Dabe, MC; CPT Denis Bouvier, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; Howard Davidson, M.D.

**Keywords:** Hodgkin's Disease, chemotherapy

**Start Date:**  
7/15/1988

**Est. Completion Date:**  
Jun 91

**Periodic Review:**  
6/7/2002

**Study Objective:** To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP-->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

**Technical Approach:** Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study. MOPP: Nitrogen mustard, 6 mg/m<sup>2</sup> IV, days 1 and 8, Vincristine, 1.4 mg/m<sup>2</sup> IV, days 1 and 8, Procarbazine, 100 mg/m<sup>2</sup> PO per day x 14 days, Prednisone 40 mg/m<sup>2</sup> PO per day x 14 days. ABVD: Adriamycin, 25 mg/m<sup>2</sup> IV, days 1 and 15, Bleomycin, 10 units/m<sup>2</sup> IV, days 1 and 15, Vinblastine, 6 mg/m<sup>2</sup> IV days 1 and 15, DTIC, 375 mg/m<sup>2</sup> IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m<sup>2</sup> IV, day 8; bleomycin, 10 units/m<sup>2</sup> IV day 8; and vinblastine, 6 mg/m<sup>2</sup> IV, day 8.

**Progress:** This study closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and continued to be followed during FY02.

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 89/080      **Status:** Ongoing

**Title:** SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Nodes and Positive Hormone Receptors

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; Howard Davidson, M.D.; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

**Keywords:** cancer:breast,chemoendocrine therapy,CAF,tamoxifen

**Start Date:**  
9/15/1989

**Est. Completion Date:**  
Sep 99

**Periodic Review:**  
7/11/2002

**Study Objective:** To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

**Technical Approach:** Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

**Progress:** This study closed to patient entry 1 Aug 95. Seven patients enrolled in this study at MAMC, three remain alive and on follow up during FY 02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 91/087                  | <b>Status:</b> Ongoing              |
| <b>Title:</b> SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954   |  |                                     |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                     |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; LTC James S. D. Hu, MC; MAJ Paul C. Sowray, MC  |  |                                     |
| <b>Keywords:</b> lymphoma:tissue procurement   |  |                                     |
| <b>Start Date:</b><br>8/2/1991   | <b>Est. Completion Date:</b><br>Aug 95 | <b>Periodic Review:</b><br>6/7/2002 |
| <b>Study Objective:</b> To acquire fresh snap-frozen lymphoma tissue to establish a central lymphoma tissue repository; to establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group; to use repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status; and to determine if pretreatment phenotype or genotype predict patient outcome with respect to complete response rate, time to progression, and survival using prospective trial designs.  |  |                                     |
| <b>Technical Approach:</b> Patients will be treated according to guidelines outlined in the specific SWOG studies. Treatment decisions will not be based on findings of the Central Lymphoma Laboratory, although clinical variables will be correlated with laboratory findings. The tissue samples will be taken from the pretreatment diagnostic biopsy or rebiopsy based on clinical decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (hematoxylin and eosin) histologic section with accompanying pathology report. The H&E stained slide and report will accommodate morphologic correlation with immunologic findings. Tissue section analysis will be performed at the University of Arizona using three stage immunohistochemistry. Future molecular studies entailing hybridization studies of RNA and DNA fragments using DNA probes will be performed as outlined in future protocols. |  |                                     |
| <b>Progress:</b> This is a companion study using tissue from other SWOG protocols. Tissue has been collected on three patients enrolled. Two patients continued to be followed during FY02. This study is permanently closed to enrollment.  |  |                                     |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 90/027      **Status:** Ongoing

**Title:** SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; Howard Davidson, M.D.; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

**Keywords:** cancer:breast,chemotherapy,chemohormonal therapy,premenopausal

**Start Date:**  
1/19/1990

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
12/2/2002

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** 11/12/2002: 10/7/2002: This study closed to patient entry 15 Feb 94. Six patients enrolled at MAMC in previous years. Two patients are deceased, four continued to be followed.

### Detail Summary Sheet

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|--|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 91/067                  | <b>Status:</b> Completed            |
| <b>Title:</b> SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients   |  |                                     |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                     |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; Howard Davidson, M.D.; MAJ Paul C. Sowray, MC; MAJ Everardo E. Cobos Jr., MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Patrick L. Gomez, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC  |  |                                     |
| <b>Keywords:</b> cancer:head & neck,cytometry,DNA  |  |                                     |
| <b>Start Date:</b><br>6/14/1991  | <b>Est. Completion Date:</b><br>Jun 94 | <b>Periodic Review:</b><br>5/9/2002 |
| <b>Study Objective:</b> To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.  |  |                                     |
| <b>Technical Approach:</b> Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck. |  |                                     |
| <b>Progress:</b> Permanent closure per SWOG, effective 1 Sep 02. All therapeutic studies providing registrations for this study have permanently closed; therefore, this study has been permanently closed. Four MAMC patients have been enrolled in this study in previous years. One patient is deceased and the other three patients continue to be followed under their therapeutic protocols.   |  |                                     |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 90/029      **Status:** Ongoing

**Title:** SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History Follow-up Study in Low-Risk, Node Negative Patients

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; LTC Kenneth A. Bertram, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; Howard Davidson, M.D.; LTC Robert L. Sheffler, MC; MAJ Rajat Bannerji, MC

**Keywords:** cancer:breast,chemotherapy,endocrine therapy

**Start Date:**  
1/19/1990

**Est. Completion Date:**  
Jan 93

**Periodic Review:**  
12/2/2002

**Study Objective:** To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

**Technical Approach:** Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

**Progress:** This study closed to patient entry 15 Jan 93. Nine patients enrolled in previous years; however, two patients died and another patient was transferred. Six patients continued to be followed under this study at MAMC during FY02.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 89/021                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin + 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in Selected Patients with Duke's B or C Colon Cancer   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; COL Irwin B. Dabe, MC; MAJ Mark H. Kozakowski, MC; CPT Denis Bouvier, MC; Howard Davidson, M.D.; MAJ Everardo E. Cobos Jr., MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC   |  |                                      |
| <b>Keywords:</b> cancer:colon,resection,chemotherapy,leucovorin,levamisole  |  |                                      |
| <b>Start Date:</b><br>2/17/1989   | <b>Est. Completion Date:</b><br>Feb 92 | <b>Periodic Review:</b><br>1/22/2002 |
| <b>Study Objective:</b> To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.  |  |                                      |
| <b>Technical Approach:</b> Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/ mesenteric implants resected enbloc (yes/no); and obstruction (yes/no). RANDOMIZE TO: (1) Observation; (2) Leucovorin 20 mg/m2 + 5-FU 425 mg/m2; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m2 + 5-FU 600 mg/m2; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole). |  |                                      |
| <b>Progress:</b> Sixteen patients enrolled at MAMC prior to closure to patient entry, 30 Jul 92. Seven patients have died from their disease and nine continued to be followed during FY02.   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 91/089 | <b>Status:</b> Ongoing |
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**Title:** SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816

**Principal Investigator:** MAJ Patrick Williams, MC

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**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; LTC James S. D. Hu, MC; LTC Luke M. Stapleton, MC

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**Keywords:** lymphoma:serum repository

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**Start Date:**

8/2/1991

**Est. Completion Date:**

Aug 95

**Periodic Review:**

6/7/2002

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**Study Objective:** To establish a central lymphoma serum repository that will serve as a resource to provide specimens for current and future scientific studies and to utilize the Southwest Oncology Group clinical data base to perform clinicopathologic correlations with the results of those studies.

**Technical Approach:** No therapy will be utilized in this study and patient treatment will not be based on this study. Patients must meet the eligibility criteria and be registered to one of the following SWOG protocols: 8516, 8809, 8736, or 8816. Ten cc's of blood will be drawn prior to protocol treatment and shipped to the SWOG Lymphoma Serum Repository at Loyola University Medical School.

**Progress:** This is a companion protocol to other SWOG protocols. Two specimens have been submitted in previous years. Those patients continued to be followed during FY02 on the treatment study.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 90/056                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; Howard Davidson, M.D.; LTC Robert L. Sheffler, MC; LTC John A. Vaccaro, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC  |  |                                      |
| <b>Keywords:</b> cancer:testicular,chemotherapy,cisplatin,bleomycin,ifosfamide   |  |                                      |
| <b>Start Date:</b><br>3/16/1990  | <b>Est. Completion Date:</b><br>Mar 93 | <b>Periodic Review:</b><br>1/31/2002 |
| <b>Study Objective:</b> To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.   |  |                                      |
| <b>Technical Approach:</b> Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study. |  |                                      |
| <b>Progress:</b> This study closed to patient entry, 1 Apr 92, with two patients enrolled at MAMC. One patient died, FY93, and the other continued to be followed during FY02.   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 91/094 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary

**Principal Investigator:** MAJ Patrick Williams, MC

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**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; LTC Luke M. Stapleton, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; LTC James S. D. Hu, MC; LTC Kenneth A. Bertram, MC

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**Keywords:** cancer:leukemia,cytogenetic studies

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**Start Date:**  
9/6/1991

**Est. Completion Date:**  
Aug 94

**Periodic Review:**  
7/11/2002

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**Study Objective:** (1) To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on Southwest Oncology Group protocols and at various times in the course of their treatment, (2) To estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients and (3) To provide quality control for all Southwest Oncology Group cytogenetic data.

**Technical Approach:** This is a companion protocol for all Southwest Oncology Group leukemia protocols. Bone marrow or peripheral blood specimens will be forwarded to a SWOG referral cytogenetics laboratory (Oregon Health Sciences University, Portland, Oregon is the nearest to Madigan Army Medical Center). The referral lab will return a cytogenetics report to MAMC. Specimens will be collected as outlined in each individual leukemia protocol.

**Progress:** No patients enrolled in this study at MAMC in FY02. Five patients enrolled in previous years. Three patients died, two continued to be followed during FY02. Patient enrollment continues.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 91/033                  | <b>Status:</b> Completed             |
| <b>Title:</b> SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for Patients with Local Regional Disease  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; LTC Luke M. Stapleton, MC; MAJ Paul C. Sowray, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; COL Joseph F. Homann, MC; COL Daniel G. Cavanaugh, MC; MAJ Everardo E. Cobos Jr., MC   |  |                                      |
| <b>Keywords:</b> cancer:esophagus,chemotherapy,surgery,modality therapy  |  |                                      |
| <b>Start Date:</b><br>2/1/1991   | <b>Est. Completion Date:</b><br>Jan 94 | <b>Periodic Review:</b><br>1/22/2002 |
| <b>Study Objective:</b> To compare, using a prospective controlled randomized study design, the outcomes of therapy of surgery alone versus pre and postoperative chemotherapy and surgery for patients with local regional esophageal cancer (outcome is defined as survival and relapse pattern); to assess the toxicities of a multimodality approach to esophageal carcinoma involving systemic chemotherapy and surgery (the toxicities of surgical resection as initial therapy or following chemotherapy will be assessed as operative morbidity and mortality); to compare the local and distant control rates with the two approaches and to define the pattern of failure; and to compare the impact on overall and disease free survival of multimodality therapy with surgery alone.   |  |                                      |
| <b>Technical Approach:</b> Esophageal cancer is seen in over 10,000 patients a year in the United States and only about 7% of these patients are cured as demonstrated by a five year survival. This study is designed to see whether or not giving chemotherapy will improve that survival. To be eligible patients must have histologic proof of squamous cell carcinoma of the esophagus, disease limited to the total regional area (clinical stage T1-T3, NX,MO), no prior surgery, radiation therapy, or chemotherapy, and adequate bone marrow, liver function, renal function, and pulmonary reserve. Patients must be physiologically fit for proposed chemotherapy and surgery and be greater than 18 years of age. Patients will be randomized to surgery alone, or to receive three cycles of preoperative cisplatinium and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatinium and 5-FU, starting two to six weeks after surgery. |  |                                      |
| <b>Progress:</b> Protocol was permanently closed 12/15/95. The last of the two patients enrolled in this study at MAMC died, Apr 02, closing out this protocol at MAMC.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 91/069 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9040 (CALGB-9081, INT-0014): Intergroup Rectal Adjuvant Protocol, A Phase III Study

**Principal Investigator:** MAJ Patrick Williams, MC

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**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; Howard Davidson, M.D.; LTC Kenneth A. Bertram, MC

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**Keywords:** cancer:rectum,5-Fluorouracil,leucovorin,levamisole

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| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
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6/14/1991

May 93

5/9/2002

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**Study Objective:** To determine the relative efficacy of: 5-FU; 5-FU plus leucovorin; 5-FU plus levamisole; and 5-FU plus leucovorin and levamisole when combined with pelvic radiation therapy in the treatment of Stages B-2 and C (TNM Stage II and III) rectal cancer. End points used will include local recurrence rates, probability of distant metastases, disease free survival rates, and overall survival.

**Technical Approach:** This will be a 4-armed study with the same radiation therapy program in all arms, but with varying drug regimens as listed in the objective. 5-FU with radiation therapy will comprise the control arm of the study. Patients will be randomized to treatment arms and they will be stratified by type of operation (abdominal perineal or anterior resection); nodal involvement (none, 1-3, or >3); and invasion through bowel wall or into adjacent organs (none, through muscularis propria, or adherence to or invasion of adjacent organs or structures). Each drug regimen will be given alone on days 1-5 and 29-33, followed by radiation therapy (five weeks) with concomitant chemotherapy on days 57-60 and 85-88. The chemotherapy regimen will then be repeated beginning 28 days after the completion of radiation therapy on days 1-5 and 29-33. If evidence of recurrence is obtained, protocol treatment will be discontinued and the patient followed until death. In the absence of recurrent disease, follow-up observations will be continued for a minimum of 5 years after surgery.

**Progress:** This study closed to patient entry, 22 Nov 92. Three patients enrolled in previous years, two patients continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 94/104                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma, A Phase III Pilot Study   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC  |  |                                      |
| <b>Keywords:</b> Cancer: colorectal, chemoprevention, calcium carbonate   |  |                                      |
| <b>Start Date:</b><br>5/6/1994  | <b>Est. Completion Date:</b><br>May 98 | <b>Periodic Review:</b><br>5/28/2002 |
| <b>Study Objective:</b> This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.   |  |                                      |
| <b>Technical Approach:</b> Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of adenomas or second primary carcinomas. |  |                                      |
| <b>Progress:</b> This protocol closed to patient accrual 22 Nov 98. Sixteen patients enrolled in this study at MAMC. Two patients are deceased, fourteen continued to be followed during FY02.  |  |                                      |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 97/096      **Status:** Ongoing

**Title:** SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; LTC James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

**Keywords:** Cancer:head and neck, radiotherapy, cisplatin, 5-FU

**Start Date:**  
5/16/1997

**Est. Completion Date:**  
Apr 00

**Periodic Review:**  
4/23/2002

**Study Objective:** 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.

**Technical Approach:** Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25% range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatin alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatin and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.

**Progress:** This study closed to patient entry, 29 Nov 99. Two patients enrolled in this study at MAMC and continued to be followed during FY02.

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 93/032

**Status:** Ongoing

**Title:** SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC

**Keywords:** cancer:breast, chemotherapy, bone marrow transplantation

**Start Date:**  
12/4/1992

**Est. Completion Date:**  
Nov 95

**Periodic Review:**  
10/21/2002

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and flurouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr, will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count of 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment. Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death). At measured times during the study a Breast Chemotherapy Questionnaire will be completed to separately document the changes in psychosocial function that occur on the two regimens.

**Progress:** This protocol closed to patient accrual 3 Aug 98. One patient enrolled in this study at MAMC and continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/097 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III

**Principal Investigator:** MAJ Patrick Williams, MC

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**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC

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**Keywords:** Cancer:Hodgkin's, irradiation, vinblastine, doxorubicin

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| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
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5/6/1994

Sep 01

4/23/2002

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**Study Objective:** The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA,IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

**Technical Approach:** Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

**Progress:** This study closed to patient entry, 24 Apr 00, when accrual goal was reached. Two patients enrolled in this study in FY94. One patient died in FY97 and the other patient continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 93/097                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9205: Central Prostate Cancer Serum Repository Protocol   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Robert L. Sheffler, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; MAJ Timothy P. Rearden, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC   |  |                                      |
| <b>Keywords:</b> Cancer:prostate, serum repository   |  |                                      |
| <b>Start Date:</b><br>5/7/1993   | <b>Est. Completion Date:</b><br>Mar 95 | <b>Periodic Review:</b><br>5/28/2002 |
| <b>Study Objective:</b> 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.  |  |                                      |
| <b>Technical Approach:</b> This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols. All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator. |  |                                      |
| <b>Progress:</b> Four patients were enrolled during FY02 for a total of 8 since study approval. Three patients have died. Five continue to be followed.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 93/136 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; LTC Robert D. Vallion, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; LTC James S. D. Hu, MC; MAJ Timothy P. Rearden, MC

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**Keywords:** cancer:non-small cell lung, 13-cis retinoic acid

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**Start Date:**

7/2/1993

**Est. Completion Date:**

Jul 98

**Periodic Review:**

5/9/2002

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**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** The protocol closed to patient accrual 9 Apr 97. Ten patients enrolled in this study. One patient was transferred to Keesler, four patients died, five patients continue to be followed at MAMC.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 93/092                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; LTC James S. D. Hu, MC; CPT Diana S. Willadsen, MC  |  |                                      |
| <b>Keywords:</b> cancer:lymphoma, tissue procurement   |  |                                      |
| <b>Start Date:</b><br>4/2/1993   | <b>Est. Completion Date:</b><br>May 95 | <b>Periodic Review:</b><br>3/21/2002 |
| <b>Study Objective:</b> 1. To acquire fresh snap-frozen lymphoma tissue from patients who relapse or have recurrent disease after being treated on Southwest Oncology Group treatment protocols. 2. To establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group. 3. To use the repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status. 4. To examine the biology of therapy failure in relationship to changes in pretreatment and post-therapy immunophenotypic data. |  |                                      |
| <b>Technical Approach:</b> Fresh frozen tissues will be acquired from relapsed patients for basic science protocols, both current and future, designed to better define the biology of relapsed non-Hodgkins's lymphoma. This is not a treatment protocol, nor will results be used to guide treatment decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (Hematoxylin and Eosin) histologic section with accompanying pathology report to The Department of Pathology at the University of Arizona in Tucson.   |  |                                      |
| <b>Progress:</b> This companion study remains open to enrollment at MAMC. No patients enrolled during FY02.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 93/166 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ John R. Caton, MC; MAJ Richard F. Williams, MC

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**Keywords:** cancer:colon, irradiation, levamisole, 5-FU

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**Start Date:**  
9/3/1993

**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
6/7/2002

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**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T4BN0-2 colon cancer and selected patients with T3N1-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** This study closed to patient entry, 17 Dec 96. One patient enrolled in this study at MAMC in FY95 and continued to be followed during FY02.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 94/111                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + Levamisole Prior to and Following Combined Pelvic XRT + Bolus 5-FU + Leucovorin in Patients with Rectal Cancer, Phase III Intergroup  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC  |  |                                      |
| <b>Keywords:</b> Cancer:rectal, 5-FU, Leucovorin, Levamisole, radiotherapy  |  |                                      |
| <b>Start Date:</b><br>5/6/1994  | <b>Est. Completion Date:</b><br>May 98 | <b>Periodic Review:</b><br>4/22/2002 |
| <b>Study Objective:</b> 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protacted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatrment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival.2) To obtain descriptive information regarding relapse patterns and tolerance.  |  |                                      |
| <b>Technical Approach:</b> Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 mg/M2/d) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to an following chemo-radiotherapy as follows: Arm A: bolus IV injection of 5-FU aloneb. Arm B: protracted venous infusion of 5-FU alone; Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvid radiotherapy. After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years. |  |                                      |
| <b>Progress:</b> This study closed to patient entry Sep 00. Four patients enrolled in this study at MAMC. One patient died in FY96. Three patients continued to be followed during FY02.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/170 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast Cancer Patients with 0-3 Positive Nodes

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

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**Keywords:** cancer:breast, chemotherapy, cyclophosphamide, doxorubicin, positive nodes

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**Start Date:**

9/21/1994

**Est. Completion Date:**

Sep 98

**Periodic Review:**

7/11/2002

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**Study Objective:** 1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide. 2) To obtain tumor tissue for biologic studies.

**Technical Approach:** Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

**Progress:** The protocol closed to patient entry, 1 May 97. One patient enrolled in this study at MAMC and continued to be followed during FY02.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 94/121

**Status:** Ongoing

**Title:** SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell Lung Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; COL Walter G. Graves, MC; LTC Maceo Braxton Jr, MC; LTC Blaine R. Heric, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; LTC Luke M. Stapleton, MC; Howard Davidson, M.D.; LTC Robert D. Vallion, MC

**Keywords:** Cancer:non-small cell lung, chemotherapy, radiotherapy, surgical resection

**Start Date:**  
6/3/1994

**Est. Completion Date:**  
Jun 98

**Periodic Review:**  
5/9/2002

**Study Objective:** 1) Assess whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year) survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer. 2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases. 3) To obtain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

**Technical Approach:** Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/M2 IVPB days 1, 8, 29, 36 and VP-16 50 mg/M2 IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II). Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5- year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

**Progress:** Two patients enrolled in FY95; however, both patients are now deceased. One patient enrolled in this study in FY00 and continues to be followed; however, this patient has recurrence of disease. Study closed to patient entry, 15 Nov 01.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 95/003 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Keywords:** cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes

**Start Date:**  
10/21/1994

**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
9/24/2002

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress:** This study closed to patient accrual, 10 Sep 96. One patient enrolled in FY96 and continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 95/093                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; CPT Diana S. Willadsen, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC   |  |                                      |
| <b>Keywords:</b> Cancer:oligodendroglioma, radiotherapy, CCNU, vincristine, procarbazine, vincristine  |  |                                      |
| <b>Start Date:</b><br>3/17/1995  | <b>Est. Completion Date:</b><br>Feb 99 | <b>Periodic Review:</b><br>1/31/2002 |
| <b>Study Objective:</b> 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe (= grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.   |  |                                      |
| <b>Technical Approach:</b> This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy ± PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA. |  |                                      |
| <b>Progress:</b> No patients enrolled in this study at MAMC in FY02. One patient enrolled in FY00 and continues to be followed. Patient enrollment continues.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/163 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; Howard Davidson, M.D.; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; LTC James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Keywords:** cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes

**Start Date:**

9/21/1994

**Est. Completion Date:**

Sep 98

**Periodic Review:**

7/11/2002

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** This protocol closed to patient accrual, 15 Apr 97. Nine patients enrolled at MAMC. Four patients have died, five continued to be followed during FY02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 97/134                  | <b>Status:</b> Completed            |
| <b>Title:</b> SWOG 9419: Tumor Tissue Biopsy for Thymidylate Synthase Expression in Patients with Colorectal Cancer, Ancillary  |  |                                     |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                     |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; LTC James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC   |  |                                     |
| <b>Keywords:</b> Cancer:colorectal, thymidylate synthase  |  |                                     |
| <b>Start Date:</b><br>8/15/1997   | <b>Est. Completion Date:</b><br>Apr 01 | <b>Periodic Review:</b><br>6/7/2002 |
| <b>Study Objective:</b> 1) To measure thymidylate synthase (TS) expression by polymerase chain reaction in tumor biopsies prior to initiation of fluorinated pyrimidine based therapy in patients with disseminated colorectal cancer and correlate tumor response with level of TS expression; 2) To correlate TS expression in tumor tissue obtained during a potentially curative resection and disease-free survival in patients with Stage II and III large bowel cancer prior to receiving adjuvant therapy with 5-FU based regimen on targeted Southwest Oncology Group trials.  |  |                                     |
| <b>Technical Approach:</b> Tissue samples from patients already on other SWOG protocols will be used. These protocols are: SWOG 9250, SWOG 9303, SWOG 9304, SWOG 9415, and SWOG 9420. Patient treatment will not be affected by registration on this protocol. TS expression will be measured using polymerase chain reaction. The following comparisons will be made: The relationship of TS expression (which may be the most important determinant of whether 5-FU will be effective) with tumor response in the disseminated setting and the relationship of TS expression with recurrence free survival in the post-operative adjuvant patients. |  |                                     |
| <b>Progress:</b> Investigators reported closure of this study at MAMC, effective 25 Jun 02. All therapeutic studies providing registrations for this study have permanently closed; therefore, this study has been permanently closed. Five MAMC patients enrolled in this study in previous years and continue to be followed under their therapeutic protocols.   |  |                                     |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/039 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9431: Cytogenetic, Molecular, and Cellular Biology Studies in Metastatic Melanoma Patients, Ancillary

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ Richard F. Williams, MC; MAJ Matthew P. Jones, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

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**Keywords:** Cancer: melanoma, metastatic, molecular studies, cellular studies

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**Start Date:**  
1/16/1998

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
11/27/2001

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**Study Objective:** (1) To characterize the frequency of non-random cytogenetic abnormalities in regional and distant melanoma metastases (AJCC Stage III or IV) and explore their association with clinical outcome of melanoma patients enrolled onto Southwest Oncology Group trials; (2) to characterize the frequency of specific genetic alterations at either the DNA, mRNA, or protein level and explore the association of these abnormalities with clinical outcome in patients with regional and distant metastases (AJCC Stage III or IV) who are enrolled on Southwest Oncology Group melanoma trials. The specific genes to be studied in this protocol will initially include: p16 (MTS1), nm23; (3) to characterize the host immunologic response to metastatic melanoma by determining whether the in vitro pattern of cytokine expression is consistent with specific subsets of T helper cells (TH1 or TH2) within melanoma deposits. To explore whether host immunologic response varies based on the site of metastatic disease and/or correlates with clinical outcome in patients enrolled on Southwest Oncology Group trials; (4) To obtain peripheral blood, sera and paraffin embedded tumor blocks from patients with metastatic melanoma to create a tissue, cell and sera bank for future studies.

**Technical Approach:** Following informed consent, tissue and blood samples taken from biopsies will be sent to a special laboratory for storage and scientific testing.

**Progress:** No patients enrolled in this study during FY02 at MAMC. Patient enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 98/113                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9444: Gastrointestinal Tumor Repository Protocol, Ancillary  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC |  |                                      |
| <b>Keywords:</b> Cancer: gastarointestinal, tumor repository  |  |                                      |
| <b>Start Date:</b><br>9/15/1998   | <b>Est. Completion Date:</b><br>Apr 02 | <b>Periodic Review:</b><br>9/24/2002 |

**Study Objective:** 1) To establish a central gastrointestinal tumor repository to serve as a tissue resource for current and future scientific studies, 2) to utilize the Southwest Oncology Group clinical database to perform clinicopathologic correlation with the results of those studies, and 3) to test new hypotheses as they emerge.

**Technical Approach:** Tissue samples obtained during biopsies will be forwarded to a special laboratory for storage and scientific testing.

**Progress:** One patient enrolled in the study in FY98 and continues to be followed under the treatment protocol. No patients enrolled in this study at MAMC in FY02. Patient enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 96/095 | <b>Status:</b> Ongoing |
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**Title:** SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; LTC James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

**Keywords:** Cancer:breast, lymph nodes, positive receptors, tamoxifen, fenretinide

**Start Date:**  
4/19/1996

**Est. Completion Date:**  
May 99

**Periodic Review:**  
3/21/2002

**Study Objective:** 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

**Technical Approach:** The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

**Progress:** This study closed to patient entry, 1 Nov 99, due to low patient accrual. Four patients enrolled in this study at MAMC and continued to be followed in FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 96/118                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; CPT Brent L. Kane, MC; LTC Kenneth A. Bertram, MC  |  |                                      |
| <b>Keywords:</b> Cancer:head and neck, surgery, radiotherapy, cisplatinum   |  |                                      |
| <b>Start Date:</b><br>5/17/1996   | <b>Est. Completion Date:</b><br>Jun 00 | <b>Periodic Review:</b><br>4/23/2002 |
| <b>Study Objective:</b> 1) To determine the efficacy of concurrent cisplatinum and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.  |  |                                      |
| <b>Technical Approach:</b> In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatinum with concurrent radiation therapy may help in local control. This data comes from in vitro as well as in vivo data showing cisplatinum may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatinum and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity. |  |                                      |
| <b>Progress:</b> The study was reactivated, 24 Apr 01, to continue follow-up on one patient enrolled in this study in FY96 at MAMC. This patient had been thought lost to follow-up, 23 May 00, and the protocol reported to the IRB as completed at that time.   |  |                                      |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 98/112      **Status:** Ongoing

**Title:** SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

**Keywords:** Cancer: colon, monoclonal Antibody 17-1A, adenocarcinoma

**Start Date:**  
9/15/1998

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
7/11/2002

**Study Objective:** (1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer, (2) to evaluate a panel of prognostic markers, in order to correlate these measures with survival and recurrence after adjuvant therapy in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer. The specific aims of the companion study will be: (a) to determine whether alterations in the expression of cell cycle related genes (thymidylate synthase, p53, and the cyclin-dependent kinase inhibitors p21 and p27) predict the risk of survival and recurrence in this patient population, (b) to determine whether alterations in markers of metastatic potential-expression of DCC and measures of tumor angiogenesis (microvascular density and vascular endothelial growth factor expression)-predict the risk of survival and recurrence in this patient population, (c) to determine whether a marker of cellular differentiation-sucrase isomaltase-predicts the risk of survival and recurrence in this patient population, and (d) to determine whether interactions among these tumor markers identify subsets of patients with significantly altered outcome.

**Technical Approach:** Subjects will be randomized and assigned to one of two treatment groups following standard surgical removal of their tumor. Group 1 will receive standard care which is surgery with no additional therapy after the tumor has been removed. Subjects will continue with routine check-ups, doctor visits and test. Group 2 will receive five antibody treatments using MoAb 17-1A. Subjects will receive the drug by as an intravenous infusion over a 2-hour time period once each 28 days. This 2-hour infusion will be repeated every 4 weeks for a total of 5 treatments. During treatment, various blood tests and x-rays will be used to determine whether the disease has returned. With subject's approval, tissue, body fluids, and other specimens obtained during the normal course of treatment will be forwarded to a special research laboratory for storage and scientific testing. Subjects will also be asked to complete a background information form to help define groups of patient being treated.

**Progress:** One patient enrolled in this study in FY98 at MAMC and continues to be followed. No patients enrolled in FY02. Study closed to enrollment, 31 May 02.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 99/014

**Status:** Ongoing

**Title:** SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

**Keywords:** Breast cancer, doxorubicin, paclitaxel, cyclophosphamide, G-CSF, tamoxifen, sequential chemotherapy

**Start Date:**  
12/15/1998

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
12/2/2002

**Study Objective:** (1) To compare sequential chemotherapy with Doxorubicin, Paclitaxel, and Cyclophosphamide to combined Doxorubicin and Cyclophosphamide followed by Paclitaxel for disease-free and overall survival, (2) to determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy courses from 21 to 14 days) will improve disease-free and overall survival, and (3) to compare the toxicity for patients treated with sequential Doxorubicin, Paclitaxel, and Cyclophosphamide with toxicity for patients with concurrent Doxorubicin plus Cyclophosphamide followed by Paclitaxel at 14 and 21 day intervals.

**Technical Approach:** This is a randomized comparison of several aggressive combination chemotherapy regimens in the treatment of high-risk breast cancer due to positive lymph nodes. It compares the current standard of care for node positive breast cancer with several more aggressive variations. All patients will receive the same number of drugs and the same amount of drugs, but the order in which the drugs are given and the time between treatments (2 weeks versus 3 weeks) will be different. Arm 1, patients will receive Doxorubicin once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses followed by Cyclophosphamide once every 3 weeks x 4 total doses. Arm 2, patient will receive Doxorubicin once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses followed by Cyclophosphamide once every 2 weeks x 4 total doses. Arm 3, patients will receive Doxorubicin and Cyclophosphamide once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses. Arm 4, patients will receive patients will receive Doxorubicin and Cyclophosphamide once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses. G-CSF and Ciprofloxacin will be given concurrent with each arm to help ameliorate side effects of the treatments.

**Progress:** 10/7/2002: This study closed to patient accrual, 31 Mar 99. Three patients enrolled at MAMC in FY99 and continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/036 | <b>Status:</b> Ongoing |
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**Title:** SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

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**Keywords:** cancer; Breast, paclitaxel, docetaxel, axillary node-positive

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**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
1/22/2002

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**Study Objective:** (1) To determine whether docetaxel improves disease-free survival and overall survival when compared to paclitaxel following 4 cycles of doxorubicin-cyclophosphamide therapy (2) To determine whether weekly administration of taxanes (paclitaxel or docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with the conventional (every 3 weeks) schedule for 4 cycles following 4 cycles of doxorubicin-cyclophosphamide therapy (3) To compare the toxicity of docetaxel given weekly for 12 weeks to that of paclitaxel given every 3 weeks for 4 cycles (4) To compare the toxicity of paclitaxel given weekly for 12 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles (5) To compare the toxicity of paclitaxel given every 3 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles and (6) To compare the toxicity of paclitaxel given weekly for 12 weeks to that of docetaxel given weekly for 12 weeks.

**Technical Approach:** This study compares aggressive chemotherapy schedules to standard of care for high risk node positive breast cancer. Eligible patients will be randomized into one of four treatment arms: Arm A, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (the standard treatment); Arm B, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (lower dose than standard); Arm C, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (medium dose); and Arm D, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (low dose).

All Arms will receive adriamycin and cyclophosphamide, IV once every 3 weeks for 4 cycles. Then Arm A will receive taxol, IV once every 3 weeks for 4 treatments. Arm B will receive taxol IV once a week for 12 weeks of treatment. Arm C will receive Taxotere IV once every 3 weeks for 4 treatments. Arm D will receive taxotere once a week for 12 weeks of treatment.

**Progress:** Two patients enrolled to this study during FY02 for a total of 14. All have completed treatment and are now on follow-up status. Study accrual goals reached and study was closed to enrollment, 8 Jan 02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/071                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC  |  |                                      |
| <b>Keywords:</b> Cancer:breast, adriamycin, taxotere, cytosan, radiotherapy  |  |                                      |
| <b>Start Date:</b><br>5/25/1999  | <b>Est. Completion Date:</b><br>Apr 03 | <b>Periodic Review:</b><br>5/14/2002 |
| <b>Study Objective:</b> To determine whether Adriamycin/Taxotere will improve disease-free survival and overall survival when compared to Adriamycin/Cytosan in lymph node positive (1-3 positive nodes) and high risk lymph node negative breast cancer. To compare toxicity of Adriamycin/Taxotere to Adriamycin/Cytosan.  |  |                                      |
| <b>Technical Approach:</b> This is multi-site study with randomization to one of two arms: Adriamycin/Taxotere (AT) or Adriamycin/Cytosan (AC). The dosages for the AT group: Adriamycin 60 mg/M2 IV and Taxotere 60 mg/M2 IV over 1 hour infusion every 3 weeks x 4 cycles. Cipro 500 mg PO b.i.d. starting Day 8 and continuing x 10 days. If a patient is allergic to Cipro, an alternative broad spectrum antibiotic may be used. Decadron 8 mg PO b.i.d., beginning one day prior to treatment with Taxotere and continued for two additional days; repeat q 3 weeks x 4 cycles. The dosages for the AC group: Adriamycin 60 mg/m2 IV and Cytosan 600 mg/ml IV. Every 3 weeks x 4 cycles. In both groups, post-menopausal patients who are ER and/or PR positive will receive Tamoxifen 20 mg PO daily x 5 years at the completion of chemotherapy. G-CSF: Patients who have an episode of febrile neutropenia should be placed on G-CSF according to ASCO Guidelines. Patients who have febrile neutropenia after a subsequent dose of chemotherapy in spite of G-CSF should have the chemotherapy doses lowered by 25%. |  |                                      |
| <b>Progress:</b> This study closed to patient entry 21 Jan 00. One patient enrolled in this study in FY99 at MAMC and continued to be followed during FY02.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/102 | <b>Status:</b> Completed |
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**Title:** SWOG E2697: Correlation of DNA Damage Index and Clinical Response in the Context of ECOG Trial E3695

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

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**Keywords:** DNA damage index, cisplatin, ECOG

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**Start Date:**

6/27/2000

**Est. Completion Date:**

Jun 03

**Periodic Review:**

6/7/2002

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**Study Objective:** To determine, using an optimized DNA-PCR assay specific for exon-6 of the glutathione S-transferase (GST-TT, gene, the extent of cisplatin-induced DNA damage in vitro in PBMC obtained from melanoma patients prior to treatment with chemotherapy or biochemotherapy and correlate the extent of DNA damage with clinical response. To determine the optimum cisplatin concentration with which to treat PBMC in vitro that will provide the highest positive and negative predictive value for response to both chemotherapy and biochemotherapy.

**Technical Approach:** This study is a companion study to SWOG E3695. Patients will have blood drawn prior to receiving chemotherapy. The peripheral blood mononuclear cells will be exposed to different concentrations of cisplatin (one of the chemotherapy drugs in E3695). The amount of cisplatin induced DNA damage will be measured. The amount of damage will be compared to the response of the tumor to chemotherapy to see if there is a correlation.

**Progress:** SWOG reported this protocol closed to enrollment, effective 18 Apr 02. MAMC IRB stipulations for approval could not be satisfied; therefore, this protocol was never initiated at MAMC.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 99/056                  | <b>Status:</b> Completed             |
| <b>Title:</b> SWOG E3695: A Randomized Phase III Trial of Concurrent Biochemotherapy with Cisplatin Vinblastine, Dacarbazine, IL-2, and Interferon A-2b versus Cisplatin, Vinblastine, Dacarbazine (CVD) Alone in Patients with Metastatic Malignant Melanoma   |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC   |  |                                      |
| <b>Keywords:</b> Cancer:non-small cell lung, carboplatin, gemcitabine, paclitaxel, cisplatin, vinorelbine, docetaxel  |  |                                      |
| <b>Start Date:</b><br>3/23/1999   | <b>Est. Completion Date:</b><br>Mar 01 | <b>Periodic Review:</b><br>1/31/2002 |
| <b>Study Objective:</b> 1) To determine whether this inpatient biochemotherapy is superior to CVD alone based on survival in patients with metastatic malignant melanoma. 2) To determine whether this inpatient biochemotherapy is superior to CVD alone based on response rate, response duration, time to treatment failure, percent CR and percent duration CR in patients with metastatic malignant melanoma. 3) To determine the feasibility of administering this in a biochemotherapy regimen to patients with metastatic malignant melanoma in a Cooperative Group setting. 4) To determine the toxicity of this inpatient biochemotherapy regimen relative to CVD alone in patients with metastatic melanoma treated in a Cooperative Group setting.  |  |                                      |
| <b>Technical Approach:</b> Each subject will be randomized to one of two arms: Arm A (CVD): Treatment will consist of Cisplatin 20 mg/m2 IV over 30 minutes. daily, days 1-4; Vinblastine 1.2 mg/m2 IV daily, days 1-4; Dacarbazine 800 mg/m2 IV over 1 hour, day 1 (only). Treatment can be administered in the outpatient setting. Cycles will be repeated every 3 weeks. Arm B (CVD + IL-2/IFN): Cisplatin 20 mg/m2 IV over 30 minutes daily, days 1-4; Vinblastine 1.2 mg/m2 IV daily, days 1-4; Dacarbazine 800 mg/ml FV over 1 hour, day 1 (only); IL-2 (Chiron) 9 MIU/m2/day by CIV, days 1-4 (96 hours); Interferon alpha 2b (Schering) 5MU/ml sc days 1-5, 8, 10 and 12; G-CSF 5 ug/kg sc qd days 7-16. All patients will be admitted to the hospital on the morning of day 1. Interferon alpha-2b, the IL-2 infusion and the rehydration for cisplatin should be planned to begin around 3 PM. Patients will be discharged ASAP after day 5 with subsequent doses of interferon to be administered in the outpatient setting or at home. Cycles will be repeated at 3 week intervals. Tumor measurements will be obtained prestudy and tumor response will be assessed after every 2 cycles. Patients with stable or responding disease will continue on therapy until disease progression, unacceptable toxicity or until they receive the maximum of 4 cycles. All patients will have renal function tests, blood counts and a thorough physical examination (including neurologic examination) prior to each cycle of chemotherapy. If abnormalities are found, these parameters will be rechecked on a weekly basis and further therapy will be withheld until laboratory values and performance status return to within the eligibility criteria (i.e., ANC > 1500/mm3, Platelets > 100,000/mm3, creatinine < 1.5, bilirubin < 1.5 and Performance Status 0 or 1). |  |                                      |
| <b>Progress:</b> SWOG reported this protocol closed to enrollment, effective 17 Apr 02. No patient enrolled in this study at MAMC.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/040 | <b>Status:</b> Ongoing |
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**Title:** SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

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**Keywords:** CHOP, monoclonal antibody, non-hodgkin's lymphoma

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**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
5/28/2002

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**Study Objective:** (1) To compare CHOP treatment with or without chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in elderly patients with diffuse mixed, diffuse large cell, and immunoblastic large cell non-Hodgkin's lymphoma of B lineage with respect to response rate, the time to treatment failure, toxicity and survival, (2) To compare IDEC-C2B8 monoclonal antibody as maintenance therapy to observation alone after CHOP chemotherapy with respect to time to treatment failure, duration of response, toxicity and survival after an initial response to induction therapy of CHOP + IDEC-C2B8, and (3) To determine if maintenance therapy with IDEC-C2B8 results in the conversion of any partial responses to a complete response.

**Technical Approach:** This study adds a new drug, chimeric anti-CD20 monoclonal antibody, to the standard treatment (cyclophosphamide, doxorubicin, vincristine and prednisone, CHOP) of Non-Hodgkin's Lymphoma. Patients eligible for this study will be randomized to receive or not to receive IDEC-C2B8 (anti-CD20) in conjunction with chemotherapy. Treatment Arm A, CHOP plus Anti-CD20 will receive the study drug IV over 6 to 12 hours on Days 7 and 3 before the first treatment cycle of CHOP. Anti-CD20 will also be given 48 hours prior to cycles 3, 5 and 7 of CHOP. Treatment Arm B will receive CHOP for a minimum of 6 or a maximum of 8 cycles. Restaging of disease after 4 cycles and again after 6 cycles will be done to determine response and eligibility to be randomized to Maintenance Treatment Arms C & D. Arm C will continue to receive Anti-CD20 IV, four weekly doses every 6 months for 2 years. Arm D will be the observation group.

**Progress:** This protocol was closed early by Hem/Onc doctors due to additional information showing one treatment is superior to the other. Two patients enrolled in this study at MAMC; 1 patient died Dec 01, and one patient completed treatment and is on follow-up.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/010                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> SWOG E5597: Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer  |  |                                       |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                       |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC  |  |                                       |
| <b>Keywords:</b> Cancer:non-small cell lung cancer, Stage I resected, chemoprevention, selenium supplementation  |  |                                       |
| <b>Start Date:</b><br>10/23/2001   | <b>Est. Completion Date:</b><br>Oct 05 | <b>Periodic Review:</b><br>10/22/2002 |
| <b>Study Objective:</b> (1) To evaluate the efficacy of selenium supplementation in reducing the incidence of second primary lung tumors in patients who have been treated for Stage I non-small cell cancer with complete surgical resection, (2) to evaluate the qualitative and quantitative toxicity of a selenium supplementation in a daily administration schedule and (3) to compare the incidence of specific cancers and mortality from cancer as well as overall survival of patients treated with selenium supplementation versus patients treated with placebo. |  |                                       |
| <b>Technical Approach:</b> Selenium chemo-prevention may improve upon patients with high risk of second lung primaries as well other aerodigestive tract tumors.   |  |                                       |
| <b>Progress:</b> The original IRB for this study was 10/23/01, there were no activity for this study the previous year. The October 22 Minutes show a continuing review was done.  |  |                                       |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 97/070 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

**Title:** SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

**Keywords:** Cancer:Non-small cell lung, Vinorelbine, Cisplatin, Observation alone, Tumour Markers

**Start Date:**  
3/21/1997

**Est. Completion Date:**  
Mar 00

**Periodic Review:**  
1/31/2002

**Study Objective:** 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.

**Technical Approach:** The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation. In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.

**Progress:** This study closed to patient entry, 30 Apr 01. One patient was enrolled and completed treatment and is now on follow-up.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/040                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC  |  |                                      |
| <b>Keywords:</b> Cancer:Breast, letrozole, five-year tamoxifen, placebo  |  |                                      |
| <b>Start Date:</b><br>2/23/1999  | <b>Est. Completion Date:</b><br>Jan 03 | <b>Periodic Review:</b><br>1/22/2002 |

**Study Objective:** Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received  $\geq 5$  years of adjuvant tamoxifen, randomized to receive wither Letrozole 2.5 mg daily or placebo daily for 5 years. Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of Letrozole with special attention to: lipid profile as assessed by blood sampling (in a limited number of centers), cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity, the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity, changes in bone density (in a limited number of centers), common toxicities as assessed by reported toxicity. Third: To evaluate overall quality of life.

**Technical Approach:** This is a multi-centre, double-blind, placebo-controlled parallel randomized trial of the NCIC Clinical Trials Group, supported by Novartis. Patients will be stratified by: receptor status at diagnosis (positive, unknown), lymph node status at diagnosis (negative, positive, unknown), and a prior adjuvant chemotherapy (yes, no). Patients will be centrally randomized to receive one of the following treatments: Arm 1 (letrozole): 2.5 mg po daily x 5 years or Arm 2 (Placebo): po daily x 5 years.

**Progress:** One patient enrolled during FY02 for a total of 13 patients. This protocol is currently ongoing for follow-up of enrolled patients only. Since approval, this study has been amended and revised a total of 8 times. All changes have been reported to and approved by the MAMC IRB.

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/121 | <b>Status:</b> Completed |
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**Title:** SWOG N9741: A Randomized Phase III Trial of Combinations of Oxaliplatin (OXAL), 5-Fluorouracil (5-FU), and Irinotecan (CPT-11) as Initial Treatment of Patients with Advanced Adenocarcinoma of the Colon and Rectum

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

**Keywords:** Oxaliplatin, 5-Fluorouracil, Irinotecan, cancer:colon, cancer:rectum

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Aug 03

**Periodic Review:**  
6/7/2002

**Study Objective:** 1) The primary objective is to compare the time to progression and overall survival in patients with locally advanced or metastatic colorectal cancer who receive one of these treatments: OXAL+5-FU+CF or CPT-11+OXAL or CPT-11+5-FU+CF (control regimen). 2) Secondary objectives include evaluation of toxicity, response rate, time to treatment failure and quality-of-life parameters in patients on the three regimens.

**Technical Approach:** This trial will compare the current standard of care for metastatic and locally advanced colon cancer to two promising new regimens. The goal is to define the new standard of care for this illness. Subjects will be randomized to receive one of three different treatments using two or three of the following 4 chemotherapy drugs: CPT-11, OXAL, 5-FU, and CF. The 3 different treatment schedules differ in the number of drugs and the amount of the drug you will receive, the amount of time over which the drugs will be given, and the length of cycles (time between doses). A complete physical to include labs, blood tests, scans and X-rays will be given at the beginning of each cycle. The 1st two cycles on the weeks you do not receive treatment, you will be contacted by telephone to talk about how you are feeling and if you are having any side effects. The treatments are as follows: Treatment A: CPT-11 will be given into a vein over 90 minutes followed by CF and 5-FU given into a vein over a few minutes, on day 1 for 4 of 6 weeks, repeated every 6 weeks. (A cycle is 6 weeks); Treatment F: OXAL will be given by vein over 120 minutes followed by CF given over 120 minutes followed by 5-FU (given over a few minutes of time) followed by 5-FU given over 22 hours. The CF and 5-FU are given on two consecutive days. Treatment is repeated every 14 days. This requires placement of an IV tube into a vein under the skin 'of the chest wall. Treatment G: OXAL will be given into a vein followed by CPT-11 over 30 minutes repeated every 3 weeks. Subject will continue same treatment until disease fails to respond to the treatment. If a complete remission is obtained, treatment may be halted and reinitiated if cancer returns. To study the treatment's effect on quality of life, participants will be asked to fill out brief forms with questions about changes in daily routines and health. This will take about 10-15 minutes. The forms will be given to the participants during their visits to the clinic. If the participant is not feeling well enough to fill out the form, a copy will be given to the participant to take home. The participant will be called within the week to go over the questionnaires and get the answers. Family members or friends are not allowed to fill out the questionnaires for the participant. Because quality of life may change over time, the participant will be asked to fill out the same form a number of times during the study (before starting the first cycle of treatment, prior to cycle two, then before every other cycle of treatment, and after the last cycle of treatment).

**Progress:** SWOG reported this protocol permanently closed to patient enrollment, effective 18 Jul 02. No patients enrolled in this study at MAMC.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/120

**Status:** Ongoing

**Title:** SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel with or without Trastuzumab as Adjuvant Treatment for Women with HER-2 Overexpressing or Amplified Node Positive Breast Cancer (an Intergroup Study)

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

**Keywords:** Doxorubicin, Cyclophosphamide, Paclitaxel, Trastuzumab, Women, HER-2, cancer:breast

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Dec 05

**Periodic Review:**  
7/23/2002

**Study Objective:** To see if the addition of Herceptin to standard AC + Taxol is beneficial for women with node positive breast cancer, whose tumors have excess amount of Her-2 gene.

**Technical Approach:** Subjects will have a full medical history and physical examination taken along with blood tests, chest x-ray, an electrocardiogram (a test that records the electrical activity of your heart), a MUGA or echocardiogram (a test that learns the function of your heart), a mammogram, and other tests that the doctor might feel are needed to fully learn about your disease. Subjects will be randomly assigned to one of three arms: Arm A - Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), Taxol by vein over 1 hour one day every week for a total of 12 treatments. Total length of treatment will be about six months. Arm B - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), you will get Taxol by vein over 1 hour one day every week for a total of 12 treatments. After all treatment with Taxol is done (about week 24), Herceptin by vein one day every week for one year. The first dose of Herceptin will be given over about 90 minutes. Subjects will be watched for 1 hour after the first dose of Herceptin. If they do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about 18 months. Arm C - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), subjects will be given Taxol, by vein over 1 hour, plus Herceptin, by vein one day every week, for a total of 12 treatments. After all treatment with Taxol plus Herceptin is done (about week 23), subjects will get Herceptin alone one day every week for six months. The first dose of Herceptin will be given over about 90 minutes. You will be watched for 1 hour after the first dose of Herceptin. If subjects do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about one year. Regardless of which treatment, at the end of all chemotherapy, subject may also get tamoxifen, if estrogen or progesterone receptor positive, for five years. If subjects had a lumpectomy, they will also get radiation therapy after chemotherapy has ended. Blood samples will be taken before the start treatment for research use. Subjects will be followed indefinitely.

**Progress:** Two patients total were enrolled on study. One was disqualified to continue with randomized Arm after initial AC course due to MUGA results. The first patient was randomized to the ARM which was to receive Trastuzumab but due to results of MUGA did not receive drug. Second patient enrolled in Apr 02 has completed the Taxol cycles and will receive 52 weeks of Trastuzumab. Patient enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/010 | <b>Status:</b> Completed |
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**Title:** SWOG R9704: A Phase III Study of Pre and Post Chemoradiation 5-FU vs. Pre and Post Chemoradiation Gemcitabine for Postoperative Adjuvant Treatment of Resected Pancreatic Adenocarcinoma

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

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**Keywords:** 5-FU, Gemcitabine, cancer:pancreatic

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**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
3/26/2002

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**Study Objective:** (1) To determine whether 5-FU based chemoradiation preceded and followed by gemcitabine improves the overall survival, local-regional and distant disease control, and/or disease free survival as compared to 5-FU based chemoradiation preceded and followed by 5-FU in the postoperative adjuvant a treatment of pancreatic carcinoma, (2) To compare the acute and late toxicities between 5-FU based chemoradiation preceded and followed by gemcitabine and 5-FU based chemoradiation preceded and followed by 5-FU and, (3) To prospectively evaluate the ability of post-resectional CA19-9 to predict survival among adjuvantly treated patients who have undergone a potentially curative resection for adenocarcinoma of the pancreas.

**Technical Approach:** This study compares two different approaches to reducing the risk of relapse after resection of pancreatic carcinoma. 5-FU plus radiation is given to both groups. Pre- and post-radiation chemotherapy is given using either 5-FU or Gemcitabine.

**Progress:** SWOG reported this study closed to enrollment, effective 26 Jul 02. MAMC enrolled one patient in this study; however the patient died of progressive disease and the protocol has now been permanently closed at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/045                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> SWOG R9811: A Phase III Randomized Study of 5-Fluorouracil, Mitomycin-C and Radiotherapy versus 5-Fluorouracil, Cisplatin and Radiotherapy in Carcinoma of the Anal Canal   |  |                         |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                         |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC   |  |                         |
| <b>Keywords:</b> fluorouracil mitomycin-c radiotherapy cisplatin carcinoma radiotherapy   |  |                         |
| <b>Start Date:</b><br>2/26/2002   | <b>Est. Completion Date:</b><br>Feb 05 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> (1) To compare initial and total local and distant failure rates in patients treated with either 5-FU + mitomycin C concurrently with RT or induction 5-FU + Cisplatin followed by 5-FU + cisplatin concurrently with RT, (2) to identify any differences in local control and colostomy rates at 2 years, (3) to determine any differences in colostomy-free, disease-free, or overall survival, (4) to compare the toxicity profiles between the two treatment arms and (5) to evaluate the prognostic effects of tumor markers P53 overexpression, human papilloma virus status and enzyme HAP1. |  |                         |
| <b>Technical Approach:</b> This study will compare standard treatment of 2 cycle combined 5 FU/Mitomycin C plus Radiation Therapy to induction 5-FU /CDDP followed by concurrent 5-FU/CDDP plus Radiation Therapy with respect to local, regional and systemic relapse and survival.  |  |                         |
| <b>Progress:</b> Ongoing for patient enrollment. No patients yet.   |  |                         |

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/044 | <b>Status:</b> Ongoing |
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**Title:** SWOG S0001: A Phase III Study of Radiation Therapy (RT) and 06-Benzylguanine (06-BG) Plus BCNU Versus RT and BCNU Alone for Newly Diagnosed Glioblastoma Multiforme (GB and Gliosarcoma)

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC John B. Halligan, MC; LTC William B. Reece, MC

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**Keywords:** Glioblastoma Multiforme, Gliosarcoma, radiation therapy, 06-Benzylguanine (06-BG), BCNU

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**Start Date:**  
2/26/2002

**Est. Completion Date:**  
Feb 05

**Periodic Review:**

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**Study Objective:** (1) To compare the overall survival, failure-free survival, and progression-free survival in patients with newly diagnosed glioblastoma multiforme (GBM) or gliosarcoma when treated with either BCNU plus radiation therapy and 06-BG, or BCNU and radiation therapy alone, (2) to assess frequency and severity of toxicities of the two treatment regimens, (3) to correlate overall survival, failure-free survival, and progression-free survival with expression of 06-alkylguanine-DNA alkyltransferase (GT) assessed with the immunohistochemistry (IHC) assay, and (4) to estimate the percentage of newly diagnosed GBM's that are AGT negative by the activity assay and explore the relationship between expression in the immunohistochemistry (IHC) assay and the activity assay.

**Technical Approach:** This study will try to determine if the depletion of AGT in GBM by O6BG in combination with BCNU and Radiation Therapy is superior with respect to survival toxicity and expression of AGT when compared to BCNU and Radiation alone.

**Progress:** No patients enrolled to this study. Remains ongoing for enrollment.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/009                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> SWOG S0003: Randomized Phase III Trial of Carboplatin and Paclitaxel Plus Tirapazamine Versus Carboplatin and Paclitaxel in Patients with Advanced Non-Small Cell Lung Cancer |  |                                       |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                       |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC   |  |                                       |
| <b>Keywords:</b> Cancer:advanced non-small cell lung cancer, paclitaxel, tirapazamine, carboplatin  |  |                                       |
| <b>Start Date:</b><br>10/23/2001  | <b>Est. Completion Date:</b><br>Nov 05 | <b>Periodic Review:</b><br>10/22/2002 |

**Study Objective:** Primary objectives: (1) To compare the effects of taxol and carboplatin plus tirapazamine to taxol and carboplatin on overall survival and progression-free survival of patients with Stage IV and selected Stage IIIB non-small cell lung cancer (NSCLC), (2) compare response rates with Stage IV and selected Stage IIIB NSCLC treated with taxol and carboplatin plus tirapazamine or taxol and carboplatin in patients with measurable disease and compare toxicities in different regimens. Secondary objectives: (1) to evaluate methylated DNA from tumor into baseline serum, at four months and after beginning treatment, checking for gene in pre-treatment tissue, (2) Evaluate protein levels of PAI1 in response to tirapazamine, and (3) obtain samples for correlative studies in future (including p27, p53 and b-tubulin).

**Technical Approach:** Few doublet/triplet combination chemotherapy regimens have substantially improved response rates and survival in advanced lung cancers. The addition of tirapazamine to carboplatin and taxol compared to carboplatin and taxol alone may improve upon standard therapy. This study will enroll patients with histological or cytological proven new diagnosed Stage IIIB or Stage IV, advanced non-small cell lung cancer.

**Progress:** Two subjects enrolled at MAMC. One patient was transferred here after receiving the 1st cycle of therapy at TAMC, and is in follow-up. A second patient enrolled in Sep 02. The study is now closed to enrollment.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/137 | <b>Status:</b> Ongoing |
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**Title:** SWOG S0012: A Comparative Randomized Study of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC

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**Keywords:** SWOG Breast cancer doxorubicin cyclophosphamide

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**Start Date:**  
9/25/2001

**Est. Completion Date:**  
Oct 04

**Periodic Review:**  
9/24/2002

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**Study Objective:** (1) To compare the microscopic pathologic response rates in patients with inflammatory and estrogen-receptor negative locally advanced breast cancer treated with weekly Doxorubicin and daily oral Cyclophosphamide given with G-CSF support to in-patients treated without "standard" Doxorubicin and Cyclophosphamide regimen given every three weeks, (2) To compare the toxicities of these two regimens, (3) To compare the delivered dose intensity of these two regimens, and (4) To assess the association between microscopic pathologic complete response and clinical complete response at the primary tumor site in these patients.

**Technical Approach:** This trial is designed to compare two different treatment regimens for breast cancer prior to surgery to see if one works better against breast cancer than the other in very poor risk patients who may benefit from up-front chemotherapy. The standard regimen of Adriamycin and Cyclophosphamide given Day 1 every 21 days is compared to a regimen of Adriamycin given once a week for 15 weeks and oral Cyclophosphamide daily for 15 weeks. Filgrastim and trimethoprim sulfa will also be given in this regimen to protect against toxicity of the chemotherapy agents used.

**Progress:** One patient enrolled in this study at MAMC during FY02. Subject enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/099                 | <b>Status:</b> Completed |
| <b>Title:</b> SWOG S0019: A Randomized Phase III Trial of ICE Chemotherapy With or Without Rituximab for the Treatment of Relapsed or Refractory CD20 Expressing Aggressive B-Cell Non-Hodgkin's Lymphomas in Patients Not Suitable For High Dose Therapy and PBSCT  |  |                          |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                          |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC    |
| <b>Associate Investigator(s):</b> MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC  |  |                          |
| <b>Keywords:</b> Cancer:B-Cell Non-Hodgkin's Lymphoma, ICE, Rituximab, relapsed lymphoma, refractory lymphoma  |  |                          |
| <b>Start Date:</b><br>5/22/2001  | <b>Est. Completion Date:</b><br>Jun 04 | <b>Periodic Review:</b>  |
| <b>Study Objective:</b> (1) To compare the progression-free and overall survival of patients with relapsed or refractory aggressive large B-cell lymphoma (CD20+) treated with three cycles of ICE (ifosfamide, carboplatin, etoposide) chemotherapy with or without concurrent treatment with four infusions of Rituximab, (2) to evaluate the unconfirmed response rate for patients treated with these regimens, and (3) to evaluate the toxicity of ICE plus four infusions of chimeric monoclonal anti-CD20 antibody Rituximab in these patients. |  |                          |
| <b>Technical Approach:</b> This study adds a new drug, ( antibody) to the ICE treatment of Non-Hodgkin's Lymphomas in patients who have relapsed or have aggressive large B-cell Non-Hodgkin's and can not be transplanted. The goal is to compare the survival and response rate of those patients treated with ICE vs ICE plus Rituximab in a patient population with poor survival status.  |  |                          |
| <b>Progress:</b> SWOG reported this protocol closed to enrollment, effective 12 Dec 01. No patients enrolled in this study at MAMC   |  |                          |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 99/019      **Status:** Ongoing

**Title:** SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool

**Principal Investigator:** MAJ Patrick Williams, MC

**Department:** Medicine/Hematology & Oncology      **Facility:** MAMC

**Associate Investigator(s):** MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

**Keywords:** Cancer, long-term follow-up, admin tool

**Start Date:**  
10/20/1998

**Est. Completion Date:**  
Indef

**Periodic Review:**  
10/22/2002

**Study Objective:** To relieve the burden on Institutional Review Boards at Southwest Oncology Group Institutions for continuing review of protocols that are closed to patient registration, and on which no patients are currently receiving protocol treatment.

**Technical Approach:** When a study has been closed to patient accrual and patients have finished treatment, it still requires submission of data to the Southwest Oncology Group to report survival and remission status and occurrence of adverse events. On an annual basis, the Southwest Oncology Group Operations Office will notify the institutions as to which protocols are eligible for transfer to the Long Term Follow-Up protocol by periodically revising the list of applicable protocols. The institutional Principal Investigator or IRB will ultimately decide for the local institution whether the protocol should be included in this protocol or continue to be reviewed on its own. A report will be prepared and submitted for annual IRB review at individual institutions. This report will include title and date closed to patient entry.

**Progress:** This protocol is an administrative tool and does not enroll patients. SWOG moves older studies to this protocol so individual IRB CR does not have to happen. There was no studies move to this study this past year. Last year the CR was done 9/25/02. The 10/22/02 minutes list this study as having yearly continuing review status. Cr paper work has been submitted earlier for this action.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/038                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG S9900: A Randomized Phase III Trial of Surgery Alone or Surgery plus Preoperative Paclitaxel/Carboplatin in Clinical Stage IB (T2N0), II (T1-2N1, T3N0) and Selected IIIA (T3N1) Non-Small Cell Lung Cancer (NSCLC)  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC   |  |                                      |
| <b>Keywords:</b> Paclitaxel, Carboplatin, cancer:lung   |  |                                      |
| <b>Start Date:</b><br>1/25/2000   | <b>Est. Completion Date:</b><br>Jan 00 | <b>Periodic Review:</b><br>1/22/2002 |
| <b>Study Objective:</b> (1) To assess whether preoperative chemotherapy with paclitaxel and carboplatin for 3 cycles improves survival compared to surgery alone in previously untreated patients with clinical Stage IB, II and Selected III A non-small cell lung cancer (NSCLC), (2) To compare operative mortality and other toxicities in the two study arms, (3) To evaluate the response rates (confirmed and unconfirmed, complete and partial) and the toxicities associated with the combination of paclitaxel and carboplatin, and (4) To obtain samples for correlation of radiologic, pathologic, molecular and biologic factors with outcome. |  |                                      |
| <b>Technical Approach:</b> This study compare surgery (the standard therapy) to chemotherapy followed by surgery to determine the standard of care for non-small cell lung cancer (NSCLC). Patients will be randomized to either surgery alone or chemotherapy (paclitaxel, IV, Day 1 every 3 weeks; carboplatin, IV, Day 1 every 3 weeks) for nine weeks prior to surgery. Chest x-rays and CT scans will be repeated to determine response to the chemotherapy and decide when the surgery should be scheduled.   |  |                                      |
| <b>Progress:</b> No patients enrolled in this study at MAMC in FY02. Patient enrollment continues.  |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/119 | <b>Status:</b> Terminated |
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**Title:** SWOG S9901: A Randomized Phase III Trial Comparing Early High Dose Chemotherapy and an Autologous Stem Cell Transplant to Conventional Dose ABVD Chemotherapy for Patients with Advanced Stage Poor Prognosis Hodgkin's Disease as Defined by the International Prognostic Factors Project on Advanced Hodgkin's Disease, Intergroup

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC

**Keywords:** Chemotherapy, Stem Cell, ABVD, Hodgkin's Disease

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Aug 03

**Periodic Review:**  
10/23/2001

**Study Objective:** 1) To compare in a cooperative group setting the progression-free survival in patients with poor prognosis advanced stage Hodgkin's disease who are treated with induction chemotherapy (ABVD X 5) followed by randomization to ABVD x 3 versus ABVD x 1 plus high dose chemotherapy plus peripheral blood stem cell rescue. 2) To compare the overall survival in this cohort of patients. 3) To compare the toxicities of these treatment regimens.

**Technical Approach:** This study will attempt to define the role of high dosed chemotherapy with stem cell transplant in the initial treatment of Hodgkin's Lymphoma. The study compares the standard of care (eight cycles of ABVD), to six cycles followed by high dose chemotherapy. Madigan expects to enroll 2 to 3 subjects per year.

**Progress:** SWOG reported this protocol closed to enrollment, effective 1 Nov 01, due to poor accrual. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/083                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG S9916: Docetaxel and Estramustine versus Mitoxantrone and Prednisone for Advanced, Hormone Refractory Prostate Cancer, Phase III  |  |                                      |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC  |  |                                      |
| <b>Department:</b> Medicine/Hematology & Oncology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC  |  |                                      |
| <b>Keywords:</b> hormone refractory prostate cancer, docetaxel, estramustine, mitoxantrone, prednisone   |  |                                      |
| <b>Start Date:</b><br>5/23/2000  | <b>Est. Completion Date:</b><br>Mar 03 | <b>Periodic Review:</b><br>6/25/2002 |
| <p><b>Study Objective:</b> (1) To compare overall survival and progression-free survival in patients with hormone refractory metastatic prostate cancer Stage D1 or D2 (with either measurable or non-measurable disease) randomized between Arm 1 (docetaxel (Taxotere®), estramustine (Emcyt®) and Arm 2 (mitoxantrone (Novantrone®) and prednisone), (2) To compare qualitative and quantitative toxicity between the two study arms, (3) To evaluate elements of Quality of Life, including: a. Palliation of metastatic bone pain and b. Global Quality of Life, (4) To record PSA values for future correlations with response and survival, and (5) To compare responses between the two treatment groups in patients with BioDimensional measurable disease.</p> <p><b>Technical Approach:</b> Subjects will be randomized to received either Treatment Arm 1, Docetaxel and Estramustine or Treatment Arm 2, Mitoxantrone plus Prednisone. Subjects in Arm 1 will receive estramustine as 2 capsules by mouth 3 x every day for 5 days plus a steroid medication by mouth on the 1st and 2nd days to decrease side effects of the docetaxel treatment. Docetaxel will be given IV on the 2nd day of the treatment course. This treatment procedure will be repeated every three weeks. Subjects in Arm 2 will receive mitoxantrone plus prednisone, by mouth twice every day for 3 weeks. The mitoxantrone treatment will be given on the 1st day, IV. This treatment procedure will be repeated every three weeks. All subjects will be asked to complete questionnaires on a regularly scheduled basis to describe the effect on their quality of life while receiving their specific treatments.</p> <p><b>Progress:</b> One patient enrolled in this study during FY02, for a total of two patients since study approval. One patient is deceased, one patient is on follow-up. Patient enrollment continues.</p> |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/084 | <b>Status:</b> Ongoing |
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**Title:** SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III

**Principal Investigator:** MAJ Patrick Williams, MC

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| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC

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**Keywords:** androgen deprivation, mitoxantrone, prednisone, high risk prostate cancer, prostatectomy

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**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
6/25/2002

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**Study Objective:** This study will evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated. Patients will be randomized to one of the following two treatment arms: (A) Casodex, + Zoladex, (B) Novantrone/Prednisone followed by Casodex, + Zoladex. This study will also compare qualitative and quantitative toxicity between the two study arms.

**Technical Approach:** This study compares standard hormonal therapy after prostate cancer surgery to standard therapy plus chemotherapy to determine the best way to prevent relapse. Subjects will be randomized to receive either Treatment 1, Hormonal Therapy which consists of Zoladex, subcutaneous injection once every 12 weeks for two years or Treatment 2, Hormonal Therapy plus Mitoxantrone plus Prednisone which consists of Zoladex subcutaneous injection once every 12 weeks for two years, Casodex taken orally once a day for two years, Mitoxantrone, IV once every 21 days for 126 days (6 cycles) and Prednisone, taken orally twice a day for 126 days. Following study completion, subjects will be followed every 6 months for two years to assess response.

**Progress:** Two patients were enrolled at MAMC during FY02 and one patient transferred here from Brooke AMC after 1st cycle, for a total of four enrolled since study initiation. Three patients are on active treatment, one in follow-up

### Detail Summary Sheet

|   |  |                                       |
|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/101                 | <b>Status:</b> Terminated             |
| <b>Title:</b> SWOG S9922: A Phase III Trial of Dexamethasone , Cyclophosphamide, Etoposide, Cisplatin (DCEP) and G-CSF with or without Thalidomide (NSC #66847) as Salvage Therapy for Patients with Refractory Multiple Myeloma  |  |                                       |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                       |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC   |  |                                       |
| <b>Keywords:</b> refractory multiple myeloma, DCEP, Thalidomide, cyclophosphamide, etoposide, cisplatin, dexamethasone  |  |                                       |
| <b>Start Date:</b><br>6/27/2000   | <b>Est. Completion Date:</b><br>Jun 04 | <b>Periodic Review:</b><br>10/23/2001 |
| <b>Study Objective:</b> 1) To evaluate and compare the overall and progression-free survival and confirmed remission rates in patients with refractory multiple myeloma treated with the DCEP regimen alone versus DCEP plus thalidomide. 2) To evaluate the qualitative and quantitative toxicities associated with these regimens.  |  |                                       |
| <b>Technical Approach:</b> Most patients with multiple myeloma, even those treated with bone marrow transplant eventually relapse. There is no standard therapy for these patients. Combination chemotherapy and thalidomide have demonstrated activity against relapsed myeloma. This trial tests whether the addition of thalidomide to combination chemotherapy provides additional benefit. |  |                                       |
| <b>Progress:</b> SWOG reported this protocol closed to enrollment, effective 1 Nov 01, due to poor accrual. No pts enrolled in this study at MAMC.  |  |                                       |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/074 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** SWOG S9925 Lung Cancer Specimen Repository Protocol, Ancillary

**Principal Investigator:** MAJ Patrick Williams, MC

|   |                       |
|---|-----------------------|
| <b>Department:</b> Medicine/Hematology & Oncology | <b>Facility:</b> MAMC |
|---|-----------------------|

**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC

**Keywords:** lung cancer specimen repository

**Start Date:**  
5/28/2002

**Est. Completion Date:**  
Nov 05

**Periodic Review:**

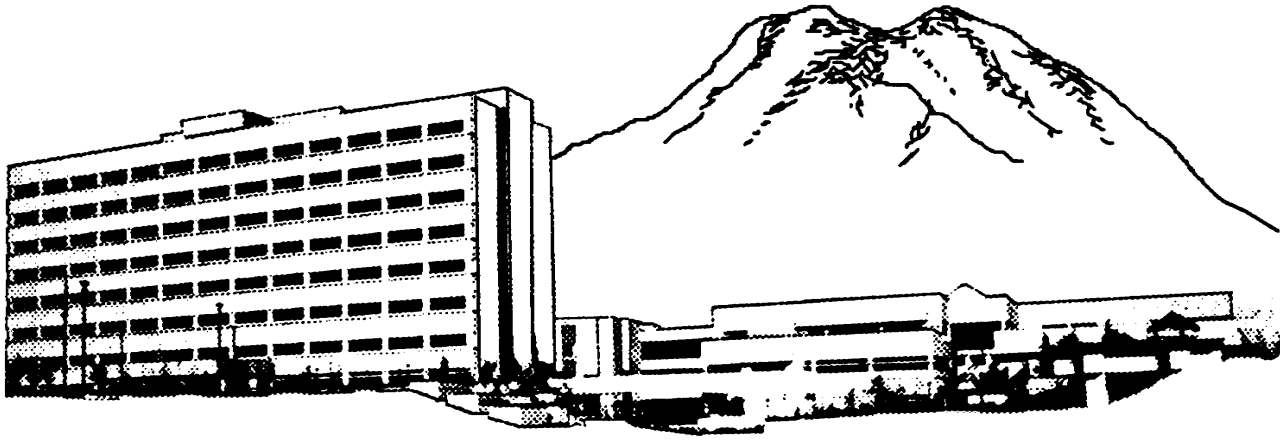
**Study Objective:** To establish a central lung cancer specimen repository to serve as a resource for current and future scientific studies. To utilize Southwest Oncology Group clinical database to perform clinic pathologic correlation with the results of those studies. To test new hypotheses as they emerge.

**Technical Approach:** Patients enrolled into select other SWOG lung cancer studies will be asked to consent to this study as well. Tissue samples will be obtained and stored.

**Progress:** This is a companion study. One patient registered during FY02. Study remains open to patient entry.

### Detail Summary Sheet

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|---|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/113                 | <b>Status:</b> Ongoing              |
| <b>Title:</b> SWOG S9927: Randomized Trial of Post-mastectomy Radiotherapy in Stage II Breast Cancer in Women with One to Three Positive Axillary Nodes, Phase III  |  |                                     |
| <b>Principal Investigator:</b> MAJ Patrick Williams, MC   |  |                                     |
| <b>Department:</b> Medicine/Hematology & Oncology   |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Inez J. Sanchez-Rivera, MC; LTC John B. Halligan, MC; MAJ Rajat Bannerji, MC   |  |                                     |
| <b>Keywords:</b> breast cancer stage II, positive axillary nodes, post-mastectomy, radiotherapy   |  |                                     |
| <b>Start Date:</b><br>7/25/2000   | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b><br>6/7/2002 |
| <b>Study Objective:</b> To compare overall and disease-free survival in pre- and post-menopausal women with Stage II breast cancer and 1-3 positive nodes treated with or without radiation therapy following mastectomy and adjuvant chemotherapy. 2) To assess local-regional control for this cohort of patients. 3). To assess the potential toxicities of radiotherapy delivered using CT-directed treatment in this cohort of patients. |  |                                     |
| <b>Technical Approach:</b> Current standard of practice does not include radiation therapy for patients with 1 - 3 positive nodes, but older studies suggest a benefit. This study will determine whether adding radiation therapy to modern chemotherapy will improve overall survival.  |  |                                     |
| <b>Progress:</b> No patients enrolled in this study at MAMC in FY02. Subject enrollment continues.  |  |                                     |



## **Detail Summary Sheets**

### **Internal Medicine Service, Department of Medicine**



### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/120                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> The Effect of Azithromycin on C-Reactive Protein Levels Following Acute Coronary Syndromes |  |                         |
| <b>Principal Investigator:</b> CPT Colin C. Edgerton, MC   |  |                         |
| <b>Department:</b> Medicine/Internal Medicine  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> LTC James J. King, MC  |  |                         |
| <b>Keywords:</b> Azithromycin, C Reactive Protein, Acute Coronary Syndrome, Human                        |  |                         |
| <b>Start Date:</b><br>9/24/2002  | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b> |

**Study Objective:** To determine the effect of azithromycin on CRP levels after acute coronary syndromes

**Technical Approach:** After appropriate initial treatment and stabilization, the study will be explained to the patient and consent will be obtained by the CCU resident. Patients will be randomized into treatment or control groups in a blinded fashion. Two blood samples will be obtained from all participants upon inclusion in the study. Blood samples consist of a minimum 150uL collected in a red/SST tube. One sample will be sent to the Madigan Army Medical Center lab for routine determination of C reactive protein levels (CRP) on the Beckman IMMAGE system. This system determines CRP levels via rate nephelometry. With this assay, the linearity of CRP is 0.1-96 mg/dL with a sensitivity of 0.1mg/dL. The second sample will be sent to the Madigan Army Medical Center Lab for freezing at -15 to -20C for future analysis. Future analysis may include highly sensitive assay for CRP. Patients will receive Azithromycin 500mg /d for 3 days then 500mg/week for 5 weeks or placebo. Two additional blood sample sets will be drawn in an identical fashion to the initial samples. One set will be drawn 24 hours after serum troponin levels have peaked. The second set will be drawn 30 days after serum troponin levels have peaked (the measurement of serum troponin levels to peak is standard of care). These samples will be processed for determination of CRP as per the initial samples.

**Progress:** Protocol was just approved. No patient enrollment yet.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/106 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Prospective Evaluation of Perioperative Risks for Patients Undergoing Noncardiac Surgery

**Principal Investigator:** CPT Brian A. Hemann, MC

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**Department:** Medicine/Internal Medicine

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Nhan V. Do, MC; LTC Gary A. Wheeler, MC;

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**Keywords:** Preop evaluation, perioperative medicine

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**Start Date:**  
10/22/2002

**Est. Completion Date:**  
Jul 04

**Periodic Review:**

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**Study Objective:** To expand upon current understanding of perioperative medicine

**Technical Approach:** To expand upon the body of knowledge for perioperative risk assessment through a descriptive study design that would describe the incidence of complications as related to risk predictors found during patient's preoperative evaluation including cardiac tests prior to surgery and available clinical prediction rules.

**Progress:** This recently received approval and has not yet been initiated at MAMC.

### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/078                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Comparison of Electronic Consults to Telephone Consults for Workload, Satisfaction, and Clinic Efficiency, A Randomized, Controlled Trial (VPCC Substudy)  |  |                                      |
| <b>Principal Investigator:</b> CPT Patricia A. McKay, MC   |  |                                      |
| <b>Department:</b> Medicine/Internal Medicine  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> CPT Samara Rutberg, MC; LTC Gary A. Wheeler, MC; MAJ Nhan V. Do, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS  |  |                                      |
| <b>Keywords:</b> Telephone consults (T-cons), Electronic consults (E-cons), Internet, Medication refills, E-mail, Patient Education  |  |                                      |
| <b>Start Date:</b><br>3/27/2001  | <b>Est. Completion Date:</b><br>Jan 02 | <b>Periodic Review:</b><br>2/26/2002 |
| <b>Study Objective:</b> (1) Evaluate the effects of secured Internet messaging as a means for communication on efficiency and quality of care in an outpatient clinic, (1) Evaluate the impact on patient and provider satisfaction and (3) Evaluate the impact on demands for office visits.  |  |                                      |
| <b>Technical Approach:</b> This protocol is designed to measure acceptance by the health care team of patient, provider, and nursing to facilitate delivery of health care. Measure of satisfaction with electronic communication by each member of this team will be compared to traditional telephone consultation. Sub-analysis of type of communication (advice, refills, acute medical need, appointment request, etc.) will demonstrate whether e-consultation is particularly conducive or poorly suited to certain types of patient-provider communications. Also measured will be the potential shift of health care from the traditional face-to-face visit to electronic consultation visit. Such virtual visits may be particularly well suited for dissemination of information and patient education The Military Healthcare System (MHS) currently does not recognize or endorse the use of electronic communication for workload purposes. Adoption of an e-con communications system could therefore represent a significant cost-shift from the military treatment facility if current policy is not appropriately amended. This protocol will give an estimate of that cost. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods. |  |                                      |
| <b>Progress:</b> A total of 60 patients enrolled in this study at MAMC. At this point, no further patients will be enrolled and data analysis has begun.   |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/072 | <b>Status:</b> Terminated |
|------------------------|------------------------|---------------------------|

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**Title:** The Effectiveness of Outpatient Management of Hyperlipidemia Using Internet Technology, a Randomized, Controlled Trial

**Principal Investigator:** CPT Patricia A. McKay, MC

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**Department:** Medicine/Internal Medicine

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS

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**Keywords:** Disease management, Internet, Patient Education, Lipid management, Hyperlipidemia, secondary prevention

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**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Jul 01

**Periodic Review:**

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**Study Objective:** (1) Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patient with hyperlipidemia using Internet technology, (2) Show that patient compliance can be improved through personalized patient education and through meaningful interactions with their providers using the Internet as the medium for communication and delivery of information.

**Technical Approach:** The study design for this pilot study is a randomized non-blinded study. The study population are patients with hyperlipidemia who are enrolled in the Adult Primary Care Clinic Cascade team. The clinicians on the Cascade team will manage both the control and study group. Patients in the placebo group will have their hyperlipidemia managed the traditional method which includes routine office visit and phone calls. The study group will be managed with routine office augmented by VPCC e-health system. The primary end point is the change in LDL cholesterol from baseline. Secondary endpoints will include patient and provider's satisfaction, effectiveness of patient and provider education, clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and logistic regression. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods.

**Progress:** This study was terminated by the principal investigator prior to receiving final approval by USAMRMC, due to a conflicting study on hyperlipidemia.

### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/101                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Adjuvant Therapy with Folate and Vitamins B6 and C in Patients with Anemia of Chronic Renal Failure Undergoing Epoetin Therapy   |  |                                      |
| <b>Principal Investigator:</b> CPT Robert M. Perkins, MC   |  |                                      |
| <b>Department:</b> Medicine/Internal Medicine  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> COL Howard M. Cushner, MC; Christopher J. LeBrun, M.D.; SSG Janice White, NC   |  |                                      |
| <b>Keywords:</b> Epoeitin, Anemia of Chronic Renal Failure, Vitamin B6, Vitamin C, Folate  |  |                                      |
| <b>Start Date:</b><br>5/22/2001  | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b><br>4/23/2002 |
| <b>Study Objective:</b> To determine whether epogen dosing requirements can be reduced through supplementation with vitamins B6, C and folate in pre-dialysis patients undergoing epoeitin therapy for their anemia of chronic renal failure.  |  |                                      |
| <b>Technical Approach:</b> This study is a group-sequential design to determine the effect of adjuvant therapy with pyridoxine, ascorbic acid, and folate on epogen dosing. Patients enrolled in the epogen clinic who meet inclusion criteria and are not excluded by our criteria will be eligible, and patient recruitment will take place during routine evaluation in the epogen clinic before and during the stabilization period. After their target hematocrit is achieved, and weekly epogen dosing has stabilized over an eight-dose period (as determined by two monthly CBCs), patients who choose to enroll in our study will receive adjuvant therapy with pyridoxine, folate, and ascorbic acid at standard doses. For patients who enroll, we will then compare weekly epogen doses required over the next two months with those doses required during the pre-vitamin, stabilization period. The primary endpoints are epogen dose required to maintain the target hematocrit and the target hematocrit itself. |  |                                      |
| <b>Progress:</b> Eight subjects enrolled in this study at MAMC in FY02, seven in FY01, for a total enrollment of 15. An amendment to the protocol was approved, Feb 02, which extended the study period to four months. Subject enrollment continues.  |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/060 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Evaluation of Exercise-Induced Proteinuria in Patients with Underlying Glomerular Disease

**Principal Investigator:** CPT David A. Philips, MC

**Department:** Medicine/Internal Medicine

**Facility:** MAMC

**Associate Investigator(s):** Christopher J. LeBrun, M.D.; MAJ Kevin Stiles, MC

**Keywords:** proteinuria, exercise, renal biopsy

**Start Date:**  
3/26/2002

**Est. Completion Date:**  
May 02

**Periodic Review:**

**Study Objective:** To evaluate the increase in proteinuria following exercise in subjects with history of nonnephrotic range isolated proteinuria and underlying glomerular disease relative to subjects with/without isolated proteinuria and no significant underlying histologic renal disease. This data may be to design further studies that would help to clarify which patients with isolated proteinuria should undergo renal biopsy. In addition, this study will help to examine the effects of exercise on active duty soldiers with baseline renal disease.

**Technical Approach:** The pilot study will consist of 18 subjects selected from a list of active duty soldiers seen in MAMC nephrology clinic, 15 of whom have a history of persistent isolated proteinuria and who have already been given a pathological diagnosis by renal biopsy. Subjects will undergo urine and serum studies before and after exercise to meet inclusions/exclusion criteria. They will undergo a Bruce protocol GXT which will be terminated after completing Stage IV of the protocol. Spot urine protein: creatinine ratios will then be calculated and compared to pre-exercise values. The differences between patients without renal disease and with normal to minimal nonspecific changes by histology will be compared to those subjects with confirmed renal glomerular disease by descriptive statistical analysis. Histological subclass of disease severity may vary between subjects and will be determined by two independent and blinded pathologists using the IgA classification system.

**Progress:** This study recently received final approval. Work on this protocol had not been initiated during FY 02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/098                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Effects Of Seasonal Change Upon Cognitive Performance And Mood In Patients Receiving Minimal Thyroid Hormone Replacement   |  |                         |
| <b>Principal Investigator:</b> CPT Gordon K. Rainey, MC  |  |                         |
| <b>Department:</b> Medicine/Internal Medicine  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> MAJ Nhan V. Do, MC; LTC Curtis J. Hobbs, MC; MAJ David E. McCune, MC; Lawrence A. Palinkas, M.D.; H. Lester Reed, M.D.   |  |                         |
| <b>Keywords:</b> Seasonal Affective Disorder, Hypothyroid  |  |                         |
| <b>Start Date:</b><br>7/23/2002  | <b>Est. Completion Date:</b><br>Aug 03 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> To study objective measures of cognition as a function of season and thyroid hormone replacement.  |  |                         |
| <b>Technical Approach:</b> The study will require 10 hypothyroid (on stable doses of replacement therapy) and 10 euthyroid subjects age 18-75 randomly selected from patients enrolled in the APCC. Each month subjects will complete a battery of tests that measure both cognitive performance and mood. In additions serum TSH, FT3, and FT4 will be measured monthly as well. Data will be analyzed using paired sample t-tests and repeated measures of variance design to determine whether seasonal changes in thyroid function are associated with changes in mood and cognitive performance. These methods will also be used to evaluate within person changes in physiological and psychological measures between baseline, summer, and winter period. |  |                         |
| <b>Progress:</b> This study recently received final approval. Work on this protocol had not been initiated during FY 02.   |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/076 | <b>Status:</b> Ongoing |
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**Title:** The Effectiveness of Outpatient Management of Hypertension Using Internet Technology, a Randomized, Controlled Trial (VPCC Substudy)

**Principal Investigator:** CPT Richard Reed, MC

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**Department:** Medicine/Internal Medicine

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS

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**Keywords:** Disease Management, Internet, Hypertension, Patient Education, Computer based Decision Support Systems (CDSS)

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**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
2/26/2002

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**Study Objective:** (1) Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patients with hypertension using Internet technology, (2) Show that patients' compliance can be improved through personalized patient education and through meaningful interactions with their providers using the Internet as the medium for communication and delivery of information.

**Technical Approach:** The study population will include both male and female patients from the APCC Cascade team with hypertension but without advanced cardiovascular complications and age range from 18 to 75. Study design is a randomized non-blinded study. The physicians on the Cascade team will manage both the control and study group. Patients in the control group will have their hypertension managed in the traditional method, which includes routine office visits and phone calls. The study group will be managed with routine office visit but with electronic communications and a limited computer clinical support system. Since no previous study exist, this study will be considered a pilot study to determine power for additional studies if needed. The primary endpoint is the change in systolic blood pressure from baseline. Secondary endpoints will include patient and provider's satisfaction, effectiveness of patient and provider education, clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and logistic regression. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods.

**Progress:** This study has not yet begun subject enrollment.



### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 90/099                  | <b>Status:</b> Completed             |
| <b>Title:</b> Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure   |  |                                      |
| <b>Principal Investigator:</b> LTC Bernard J. Roth, MC   |  |                                      |
| <b>Department:</b> Medicine/Internal Medicine  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> LTC William H. Cragun, MC; CPT Stephen M. Salerno, MC; CPT Donald M. Collins, MC;  |  |                                      |
| <b>Keywords:</b> pleural effusion,albumin,congestive heart failure   |  |                                      |
| <b>Start Date:</b><br>8/17/1990  | <b>Est. Completion Date:</b><br>Jun 96 | <b>Periodic Review:</b><br>8/28/2001 |
| <b>Study Objective:</b> To determine if the albumin gradient is a more effective criterion than Light's criteria to distinguish transudates from exudates in patients with congestive heart failure that have been treated with diuretics.   |  |                                      |
| <b>Technical Approach:</b> Fifteen patients with clinically suspected congestive heart failure and chest radiograph evidence of pleural effusion will be studied. A thoracentesis to remove 50 cc of fluid will be performed and the following laboratory tests will be done on the fluid: albumin, total protein, glucose, LDH, bilirubin, cell count with cyto-spin differential, gram stain, and routine culture. A simultaneous sample of serum will be measured for albumin, total protein, LDH, bilirubin, and glucose. After three to five days of therapy for the congestive heart failure a repeat chest radiograph with bilateral decubitus view will be done. If pleural fluid persists, a repeat thoracentesis and laboratory tests will be done. If no fluid persists after three to five days, then the patient will be dropped from the study. Bilirubin ratio will also be assessed. The classification of the patients as exudate or transudate by serum effusion, bilirubin ratio, and Light's criteria will be compared between the two thoracentesis. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria. |  |                                      |
| <b>Progress:</b> This study was reported completed, 30 Aug 02, following the PCS of its principal investigator. Data analysis continues. An abstract of findings is not yet available.   |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/117 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Serum Cardiac Troponin Levels After Positive Cardiac Stress Tests

**Principal Investigator:** CPT Samara Rutberg, MC

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|---|-----------------------|
| <b>Department:</b> Medicine/Internal Medicine | <b>Facility:</b> MAMC |
|---|-----------------------|

**Associate Investigator(s):** LTC James J. King, MC

**Keywords:** Troponin I, Exercise Stress Test, Cardiac Ischemia

**Start Date:**  
7/24/2001

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
6/10/2002

**Study Objective:** To determine if positive cardiac stress tests lead to elevated serum troponin levels.

**Technical Approach:** Patients who present to the MAMC emergency room with chest pain and are presumed to have cardiac ischemia by history or a positive EKG for ischemia (1 millimeter ST segment depressions in two consecutive EKG leads), yet a negative initial serum troponin level, will be admitted to the inpatient ward to be ruled out for an acute myocardial infarction. Once the workup for an acute myocardial infarction is negative the patient will undergo a cardiac stress test in the Cardiology treadmill room. Twenty patients with positive cardiac stress tests will be consented for the study. All patients entered in the study will remain in the hospital and a serum troponin level will be drawn within 6 to 12 hours after their cardiac stress test. Any patient, who has ST segment elevations on their EKG during their cardiac stress test, or show concern for persistent cardiac ischemia, will be readmitted to the inpatient ward and immediately assessed by the cardiology service.

**Progress:** This study has not yet been initiated at MAMC and remains suspended pending a revised protocol based. The original protocol contained a potential negative impact on nursing staff and in-patient services.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/125                 | <b>Status:</b> Terminated            |
| <b>Title:</b> The Effect of Montelukast on the Methacholine Challenge   |  |                                      |
| <b>Principal Investigator:</b> CPT Kevin E. Schlegel, MC  |  |                                      |
| <b>Department:</b> Medicine/Internal Medicine   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> CPT David Y. Gaitonde, MC; LTC John C. Walker, MC; COL Jerry L. Pluss, MC; CPT Thomas C. Hattan, MC |  |                                      |
| <b>Keywords:</b> monteleukast, methacholine challenge, leukotriene receptor antagonists, asthma                                       |  |                                      |
| <b>Start Date:</b><br>8/28/2001   | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>7/23/2002 |

**Study Objective:** Investigate the effect of the leukotriene receptor antagonist (LTRA), montelukast, on airway hyperresponsiveness to inhaled methacholine.

**Technical Approach:** The goal of this small study is to investigate the effect of montelukast on inhaled methacholine challenge in 30 subjects with positive or borderline positive methacholine challenges. Clinical significance is whether the subject reacts to the methacholine challenge at an increased concentration, ie. does the change in reactivity bump a subject from the severe to the mild category of BHR? Subjects will be eligible to participate if they have a positive methacholine challenge (20% decline or more in FEV1 at concentrations of methacholine up to 16 mg/ml) and do not meet any of the exclusion criteria. Study subjects will be given 2 to 3 weeks of therapy with montelukast 10 mg or placebo orally once a day, then undergo a second methacholine challenge. After a two week wash out period they will perform the opposite arm of the study and undergo a third methacholine challenge. Comparison to baseline results will be made with each subject serving as his/her own control. Primarily, the concentration of methacholine required to decrease the FEV1 by 20% (PC20) before and after 2- 3 weeks of montelukast and placebo will be analyzed on an individual participant basis.

**Progress:** Two subjects enrolled in this study at MAMC in FY02. However, investigators chose to terminate the protocol based on conclusive evidence published during the study which proved their hypothesis.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/108 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Multicenter, Randomized, Double-blind, Double-dummy, Parallel Group Study to Assess the Efficacy, Safety and Tolerability of New Oral Formulation Terbinafine in Patients with Onychomycosis of the Toenails, Protocol No. CSFO327L2302

**Principal Investigator:** LTC Gary A. Wheeler, MC

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| <b>Department:</b> Medicine/Internal Medicine | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Theron M. Pettit, MC

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**Keywords:** onychomycosis; dermatophyte; terbinafine

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**Start Date:**

8/27/2002

**Est. Completion Date:**

Jul 04

**Periodic Review:**

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**Study Objective:** The primary objective of this trial is to determine if a new oral formulation of terbinafine is as effective in treating onychomycosis of the toenail as the standard terbinafine treatment is. The secondary objective is to assess the safety and tolerability of the new oral formulation terbinafine

**Technical Approach:** This multicenter clinical trial is a randomized, double-blind, double-dummy, placebo-controlled parallel-group non-inferiority study to compare new oral formulation (NOF) terbinafine to the current treatment regimen in patients with onychomycosis of the toenails. Approximately 900 subjects will be enrolled at 50 centers, with approximately 20 to 27 patients participating at MAMC. Study duration is up to 54 weeks and consists of 3 periods: Screening, Treatment, and Post-treatment Assessment. Following a screening physical and laboratory assessments, eligible patients who meet all entry criteria will be randomized to one of two treatment groups by assignment to the lowest randomization number available. The Treatment period will last 12 weeks, in 3 blinded 4-week cycles of active plus placebo tablets and/or capsules. In Treatment Weeks 4, 8, and 12, patient assessments are repeated, adverse events solicited, and drug accountability performed. Patients will be contacted by telephone between visits for monitoring. At Week 16, the end of treatment, medication is collected from patients. Post Treatment evaluations are performed at Week 24, 36, 48. Lab evaluations are completed again at week 48, the end of study, including a serum pregnancy test for women of childbearing potential. No topical or systemic antifungal therapies are allowed during the Post Treatment assessment period. Patients may elect to participate in a pharmacogenetics sub-study that will be separately consented. One 18ml blood sample will be drawn which will be shipped to the central laboratory for DNA extraction and frozen storage for future study for up to 20 years. The use of the genetic material will be limited to studying the role(s) genes play in onychomycosis and patient responses to terbinafine therapy. The primary efficacy assessment of the trial is the percentage of patients who experience complete cure of the target toenail at week 48, defined by 0% residual involvement of the target toenail as documented by photography, negative culture for dermatophytes and negative KOH microscopy, and this data will be summarized by percentages and frequencies. For exploratory purposes, clinical cure, clinical effectiveness, relapse, and physician and patient global assessments will be evaluated.

**Progress:** This study recently received IRB approval and had not yet been initiated at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/048

**Status:** Ongoing

**Title:** A Multinational, Randomized, Double-blind, Placebo-controlled, Forced-titration, 2X2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT), Protocol No. CDJN608 B2302

**Principal Investigator:** LTC Gary A. Wheeler, MC

**Department:** Medicine/Internal Medicine

**Facility:** MAMC

**Associate Investigator(s):** Marvin Y. Hayami, M.D.; CPT Cecily K. Peterson, MC; CPT Sarah A. Rodriguez, MC; MAJ Nhan V. Do, MC; Shaila B. Kode, M.D.; Kathleen K. Davis, M.D.; MAJ Theron M. Pettit, MC

**Keywords:** impaired glucose tolerance, cardiovascular risk factors, pharmacogenetics

**Start Date:**  
2/26/2002

**Est. Completion Date:**  
Aug 09

**Periodic Review:**

**Study Objective:** Core Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on the progression to diabetes in subjects with impaired glucose tolerance (IGT) at increased risk of a cardiovascular event. Extension Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on cardiovascular morbidity and mortality. Definition of this composite endpoint is provided on page 11 of the attached Protocol, and is further discussed in the Summary to this cover document.

**Technical Approach:** Approximately 24 subjects will be enrolled at MAMC. Study design projects enrollment of 7500 subjects from 600-800 centers in about 40 countries, with approximately 1875 subjects in each of 4 treatment groups. 75% of subjects will receive at least one of the study drugs. All study drugs are taken orally. Nateglinide 60 mg before meals + matching placebo once daily Nateglinide 60mg before meals + Valsartan 160mg once daily Matching placebo before meals + matching placebo once daily Matching placebo before meals + Valsartan 160mg once daily Patients will be invited to participate in screening who have one or more risk factors for the conditions under study (such as family history, known IGT, high BMI, dyslipidemia.) Eligible patients will be randomized using an electronic interactive voice recognition system. There will be Sixteen study visits after initiation of study treatment: at +2 weeks, +4 weeks, +3 months, +6 months, then visits will be every 6 months. Patients will arrive fasting, scheduled between 7-10am. Weight, blood pressure, heart rate and blood sampling is performed at each visit. A urine specimen will be collected at 3 time points. An ECG, (electrocardiogram) is performed at the second visit and repeated twice during the study. The OGTT with FPG and insulin level is completed every 12 months after baseline, at month 37 (for confirmation), and as indicated to confirm progression to diabetes. Subjects are asked to keep a diary of suspected hypoglycemic events and a subset of patients may be provided a blood glucose monitor to record these occurrences. This study will include life style intervention counseling of subjects at every visit, with written educational materials provided by the study sponsor.

**Progress:** 14 patients have been consented and screened for possible study participation. The site is finding an 88% screen-fail rate and the overall study is finding a 90% failure rate, due to OGTT results not meeting protocol inclusion criteria. One subject has been randomized and remains in follow up. The OGTT results of one person screened suggested need for evaluation for possible diagnosis of diabetes melitus. This individual has been referred back to the PCP. PCP referrals continue, and screening remains open. Protocol Amendment 2 was issued by the study sponsor, 7 Jun 02. The Amendment and revised consent form were approved by MAMC IRB in Jun 02.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/113 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Proposal for a Patient Check-in and Preventive Services Kiosk

**Principal Investigator:** LTC Gary A. Wheeler, MC

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|---|-----------------------|
| <b>Department:</b> Medicine/Internal Medicine | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Nhan V. Do, MC

**Keywords:** kiosk customer service artificial intelligence preventive health interpretations  
pharmacy renewals screening

**Start Date:**

9/24/2002

**Est. Completion Date:**

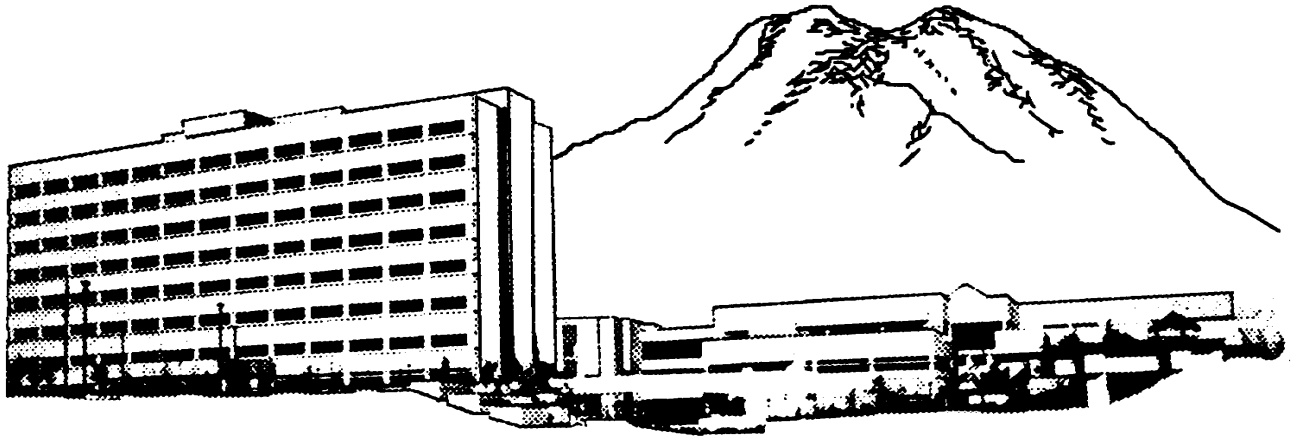
jun 03

**Periodic Review:**

**Study Objective:** To create and validate a patient-friendly Kiosk-style outpatient clinic check-in station (Automated Check-In Machine, aka ACM). The ACM will direct patients to verify their CHCS demographics and insurance information and remind patients of overdue and upcoming preventive services. The outpatient clinic encounter will thus be "pre-populated" with pertinent information before the first healthcare team member even knows the patient has arrived.

**Technical Approach:** Observation study, prospective, population-based, paired design. Baseline data for proportion of population meeting preventive services recommendations (cholesterol screening, pap smear, mammogram, colorectal cancer screening, and immunizations), satisfaction data (Quality of Health Care at the MTF, Interpersonal Relations, Waiting Times at Appointment at MTF, Overall Satisfaction with MTF Clinic Visit, Overall Satisfaction with Medical Care Received at MTF), and third party collections will be collected at the beginning of the study period, and again at the end of the study period

**Progress:** This study has not yet been initiated at MAMC waiting impact statements from affected departments/services.



## **Detail Summary Sheets**

### **Neurology Service, Department of Medicine**

## Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 200/123 **Status:** Ongoing

**Title:** Carpal Tunnel Syndrome in Pregnancy: A Prospective Study on its Natural History

**Principal Investigator:** MAJ John E Hartmann, MC

**Department:** Medicine/Neurology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Wendy Ma, MC; CPT Paul J. Walting, MC; CPT Anna M. Hohler, MC; COL Giorgio S. Turella, MC; LTC Beverly R. Scott, MC; MAJ Traci D. Ryan, MC; CPT Trenton James, MC; CPT David T. Torzala, Jr., MC; MAJ David J. Wilkie, MC; CPT Gwendolyn M. Brophy, MC

**Keywords:** carpal tunnel syndrome, pregnancy, incidence

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Sep 02

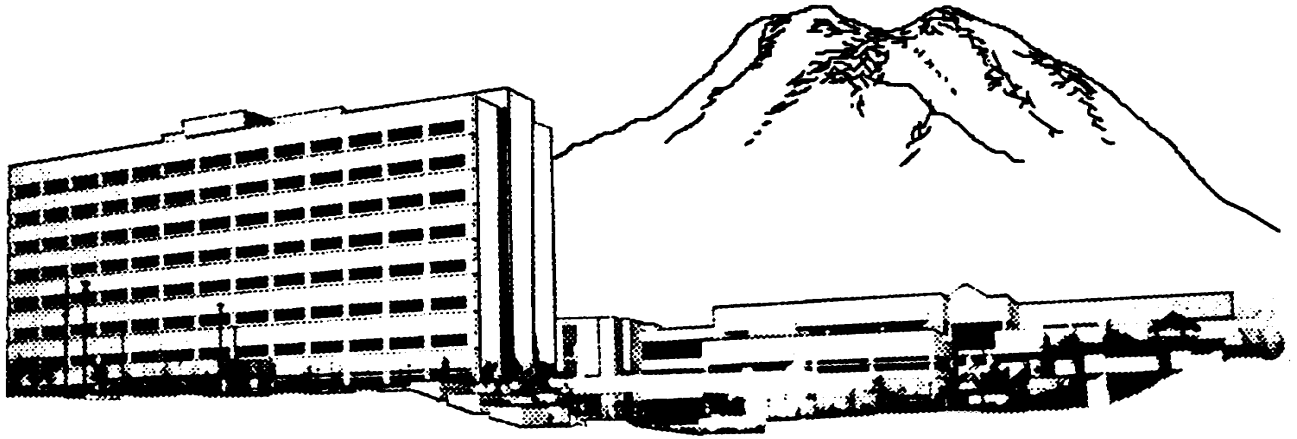
**Periodic Review:**  
6/25/2002

**Study Objective:** This study will try to determine the incidence of Carpal Tunnel Syndrome (CTS) during pregnancy in a prospective manner. Secondary objectives of this study will try to determine: (1) the incidence of CTS in each trimester of pregnancy; (2) potential risk factors for developing CTS in pregnancy such as Gestational Diabetes, preeclampsia, CTS in prior pregnancies, history of CTS prior to current pregnancy, excessive weight gain during pregnancy, nulliparous vs. multiparous pregnancies, single vs. multigestation pregnancies, concurrent hypothyroidism, and particular occupations; (3) the persistence of signs and symptoms of CTS after delivery and (4) pilot test a survey assessing Restless Leg Syndrome in pregnant women.

**Technical Approach:** This protocol will survey women seen in the Obstetric Clinic at MAMC for the development of CTS during each trimester and postpartum. Women will be enrolled at their first antepartum check and given a biographical sheet and questionnaire to complete, and an initial physical exam for the evaluation of CTS administered. The examiner will test the patient's ability to feel light touch, pinprick and 2 point discrimination at the points outlined. The examiner will then test muscle strength in the Abductor Pollicis Brevis, Opponens, Adductor Digiti Minimi, and Extensor Indicis Proprius. A Tinel's sign will be tested at each wrist, and Phalen's sign will be positive if sensory changes are reproduced in a median nerve distribution within 20 seconds of wrist flexion. At each evaluation, the presence of possible, probable, or definite CTS will be determined. Possible CTS will be defined as follows: Sensory changes to the hand, with nocturnal symptoms. Probable CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Localization by physical exam would be defined as consistent sensory findings over areas supplied by branches of the median nerve traversing through the carpal tunnel (via pinprick and light touch). Definite CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Motor findings, such as atrophy and weakness of median innervated muscles would be defined as Definite CTS. The Obstetrician will review the chart to complete the data for other obstetrical information. For the pilot study of RLS, the patient will answer questions on this topic during each of the sessions. Serial questionnaires and physical exams would be performed at the following intervals: 20-24 weeks gestation, 34-36 weeks gestation, and 6-10 weeks postpartum.

**Progress:** During FY02, 220 women enrolled in this study for a total of 503 women. No further enrollment is expected. Women who are currently pregnant and who have delivered within the past 6 weeks will continued to be followed. Data analysis for areas of significance with commence. No signifant changes to the original protocol has been made





## **Detail Summary Sheets**

### **Pulmonary Disease & Critical Care Service, Department of Medicine**

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/129 | <b>Status:</b> Ongoing |
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**Title:** Osteoporosis in Patients with Obstructive Lung Disease Who Are on Non-continuous Oral Steroid or Inhaled Steroid Therapy

**Principal Investigator:** LTC Bernard J. Roth, MC

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| <b>Department:</b> Medicine/Pulmonary&Critical Care | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT Todd C. Bennett, MC; Suzette Gagnon-Bailey, RN

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**Keywords:** osteoporosis, secondary osteoporosis, glucocorticoid therapy, intermittent glucocorticoid therapy, systemic glucocorticoid therapy, prednisone, bone mineral density,

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|---------------------------------|--|--------------------------------------|
| <b>Start Date:</b><br>8/28/2001 | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>8/27/2002 |
|---------------------------------|--|--------------------------------------|

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**Study Objective:** To determine if there is an association between intermittent systemic glucocorticoid therapy or inhaled steroid therapy and secondary osteoporosis in patients with obstructive lung disease.

**Technical Approach:** This pilot descriptive cross-sectional study will identify patients managed in the Pulmonary clinic for COPD or asthma who have received intermittent doses of oral corticosteroids within the last 6 months. Patients with COPD or asthma who have not been treated with intermittent oral steroids but are on inhaled steroids will be compared to this group. A third group of patients with COPD or asthma on chronic oral steroids will be identified and will serve as a comparison group of patients at known high risk for osteoporosis. Dual energy X-ray bone absorptiometry will be performed on all patients. The bone density of patients with intermittent oral steroid use will be compared to control patients and to patients with chronic oral steroid use.

**Progress:** This study accrued 103 participants during FY02 with a goal of about 200 patients. This study hopes to complete enrollment within 6 months.

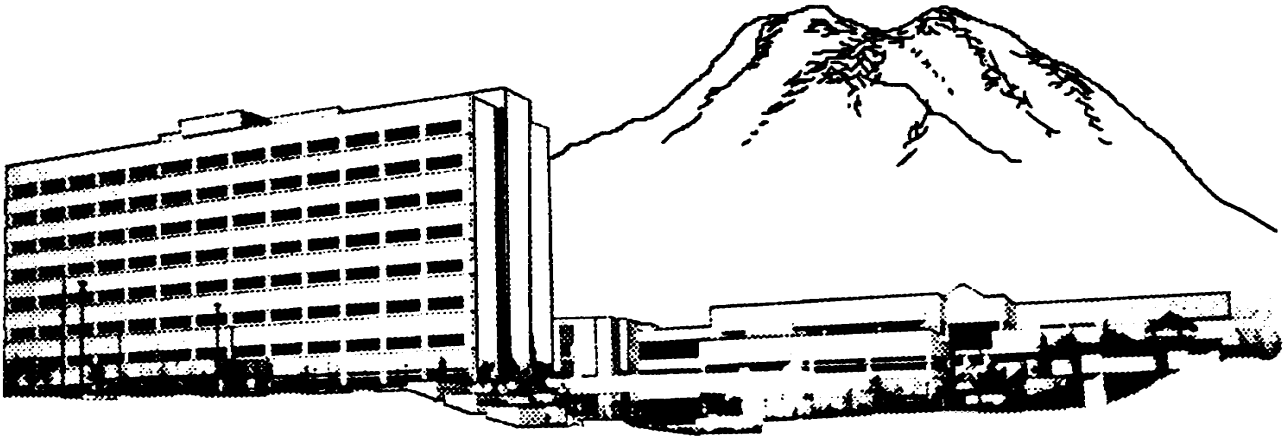
### Detail Summary Sheet

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|--|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 97/132                  | <b>Status:</b> Ongoing                |
| <b>Title:</b> Respiratory Care Team to Decrease the Misuse of Metered Dose Inhalers in Hospitalized Patients   |  |                                       |
| <b>Principal Investigator:</b> LTC Bernard J. Roth, MC   |  |                                       |
| <b>Department:</b> Medicine/Pulmonary&Critical Care  |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> COL Thomas A. Dillard, MC; Michael G. Winter, RRT; Nora A. Regan, RRT; CPT John J. Mullan, MC; CPT Michael W. Quinn, MC; CPT Won S. Song, MC |  |                                       |
| <b>Keywords:</b> Inhaler, metered dose, proper use   |  |                                       |
| <b>Start Date:</b><br>9/19/1997  | <b>Est. Completion Date:</b><br>Mar 96 | <b>Periodic Review:</b><br>10/22/2002 |

**Study Objective:** To determine if a respiratory team teaching proper metered dose inhaler (MDI) use to inpatients will improve the observed rate of proper MDI use at Madigan Army Medical Center (MAMC).

**Technical Approach:** In this study, a pulmonologist will interview 60 inpatients prescribed an MDI and observe their MDI technique to establish a baseline rate of misuse. Then a respiratory care team will receive a daily list from Pharmacy on all patients newly prescribed an MDI. They will provide direct teaching to the patients on correct use of their MDI. After the teaching program has been in place for 2- 6 weeks the same pulmonologist will interview 60 more patients and observe their MDI technique to establish the rate of misuse after the intervention. The patient will be asked if they have received education and this will be correlated to the chart documentation of education by the Respiratory Therapist. The major endpoint will be the change in the rate of MDI misuse observed.

**Progress:** The first phase of the protocol was completed during FY01. The project was stalled due to loss of respiratory therapy personnel and deployment of associate investigator, Dr. Mullen. A new associate investigator, Dr. Song, has joined the protocol and will attempt to complete the final phase of the study during FY03.



## **Detail Summary Sheets**

### **Department of Nursing**

### Detail Summary Sheet

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|---|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/074 | <b>Status:</b> Ongoing |
| <b>Title:</b> E-Health Demand Management for Frequent Medical System Utilizers (VPCC-FMU Substudy)                                |                        |                        |
| <b>Principal Investigator:</b> Pamela S. Birgenheier, RN  |                        |                        |
| <b>Department:</b> Nursing  | <b>Facility:</b> MAMC  |                        |
| <b>Associate Investigator(s):</b> COL Nancy A. Woolnough, AN; LTC Gregory A. Gahm, MS; Deland Peterson, Ph.D.; MAJ Nhan V. Do, MC |                        |                        |
| <b>Keywords:</b> E-Health, Primary Care, Nursing, Telemedicine, TRICARE Senior Prime, Health Promotion                            |                        |                        |

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| <b>Start Date:</b><br>3/27/2001   | <b>Est. Completion Date:</b><br>May 01 | <b>Periodic Review:</b><br>2/6/2002 |
| <b>Study Objective:</b> (1) Utilize the Virtual Primary Care Clinic (VPCC) infrastructure to support demand management of frequent medical system utilizers (FMU) who are presently enrolled in TRICARE Senior Prime (TSP) (2) Evaluate the effects of regular electronic communication (messages reflecting concern for patient health and health promotion information) on medical system utilization frequency for TSP patients identified as frequent medical system users and (3) Evaluate the workload requirements and appropriateness of having nursing staff implement this process.   |  |                                     |
| <b>Technical Approach:</b> This study utilizes nursing staff to implement a demand management program for TRICARE Senior Prime(TSP) patients enrolled in the APCC at MAMC. Participants will include 150 (50 treatment condition, 50 standard VPCC, 50 control) TSP patients previously identified by MAMC Utilization Management and the Northwest Lead Agent as frequent system users (10 or more outpatient visits [Specialty care, Primary care, AIC, or ER]). Control I - TSP APCC patients receiving standard care with no VPCC; Control II - TSP APCC patients receiving VPCC access without specific focused health concern or health promotion interaction; Control III - previous personal history of treatment group TSP APCC patient utilization prior to initiation of the VPCC. Nursing staff can appropriately implement this procedure. The workload requirements for nursing staff to implement this process will be more than offset by the decreased medical system utilization by patients. |  |                                     |
| <b>Progress:</b> This protocol has not yet begun subject enrollment.  |  |                                     |

### Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 201/012 **Status:** Ongoing

**Title:** In-Home Urinary Incontinence Therapy for Female Soldiers

**Principal Investigator:** Kathleen A. Clary, RN

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** Lori A. Loan, Ph.D.; COL Gary D. Davis, MC; LTC (Ret) Richard A. Sherman, Ph.D.; LTC Ann M. V. Bianchi, AN

**Keywords:** Urinary incontinence, female soldiers, access to care, military specific

**Start Date:**  
10/24/2000

**Est. Completion Date:**  
Oct 02

**Periodic Review:**  
10/22/2002

**Study Objective:** The study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for exercise-induced urinary incontinence in the home setting with those receiving similar biofeedback treatments in the Troop Medical Clinic or medical center environment. This aim will be accomplished by adding a third group (in-home biofeedback) to the two groups already enrolled (TMC & Medical Center) in the MAMC approved study, Improving Soldier Access to Urinary Incontinence Therapy (Loan, 98-053).

**Technical Approach:** This proposed study represents the investigation of an innovative evidence-based health care delivery intervention that may be successful in alleviating some of the problems related to access to care for female soldiers with exercise-induced urinary incontinence. This will be accomplished by providing portable, in-home biofeedback equipment and a 12-week nurse run biofeedback program to 62 female soldiers with exercise induced urinary incontinence. The study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for urinary incontinence in the home setting with results from those who previously received biofeedback treatments in the troop medical clinic or medical center environment. Data from 62 prospective and approximately 124 retrospective female soldiers treated with biofeedback for urinary incontinence will be used to address the following hypotheses: For female soldiers with exercise-induced urinary incontinence: (1) treatment obtained in the home environment will significantly increase realized access to care compared to treatment obtained at the troop medical clinic or the medical center; and (2) patient satisfaction will be significantly higher when treatment is received in the home environment and lower when treatment is received at the troop medical clinic or the medical center. Descriptive statistics will be used to summarize central tendency and data dispersion. Pretreatment differences in demographic and descriptive information will be compared using ANOVA or Kruskal-Wallis ANOVA for Ranks as appropriate.

**Progress:** During FY02 screening tools were sent to 761 female soldiers on Ft. Lewis with 227 returned. Screening and recruitment for this study is done jointly with MAMC Protocol #98053. Forty-two women indicated they wanted treatment for urinary incontinence, 22 were eligible, consented, and started the intervention. Sixteen soldiers completed the intervention this FY – 10 in the two groups for protocol #98053 and 6 in this study. A second mailing of the screening tool is underway.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/062                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Army Hospitals: Work Environment, Quality of Care and Intent to Leave   |  |                         |
| <b>Principal Investigator:</b> COL Eileen A. Hemman, AN   |  |                         |
| <b>Department:</b> Nursing  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> LTC Patricia A. Patrician, AN; LTC Laura R. Brosch, AN; COL Melissa A. Forsythe, AN   |  |                         |
| <b>Keywords:</b> individual attributes, work environment attributes, affective responses to the job (burnout and job satisfaction), quality of care, and intent to leave the Army workforce, military specific  |  |                         |
| <b>Start Date:</b><br>4/23/2002   | <b>Est. Completion Date:</b><br>Jun 03 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> This study proposes to: (1) Describe the individual attributes, the work environment attributes, affective responses to the job (burnout and job satisfaction), perceived quality of care and intent to leave the Army workforce from the perspective of military and civilian staff nurses working in Army hospitals. (2) Explain the relative contributions of individual attributes, work environment attributes, and affective responses to the job in explaining intent to leave the Army workforce. (3) Examine the added contribution of nurses' perceptions of the quality of care they provide to explaining intent to leave the Army workforce. |  |                         |
| <b>Technical Approach:</b> This two-year descriptive and correlational study employs a cross-sectional design to survey all military and civilian RNs assigned to inpatient units in 24 Army hospitals throughout the United States, including Alaska and Hawaii. Survey data will be used to assess work environment attributes, individual attributes, affective responses to the job, nurse-rated quality of care, and intent to leave the Army workforce.   |  |                         |
| <b>Progress:</b> A total of 210 surveys were sent on the first mailing with a 48% response rate. A second mailing of 109 surveys was completed in September. The study is currently in data analysis by the PI at WRAMC.  |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/053 | <b>Status:</b> Ongoing |
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**Title:** The Role of Mentoring in the Career Advancement of Hispanic Army Nurses

**Principal Investigator:** COL Eileen A. Hemman, AN

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| <b>Department:</b> Nursing | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL Margarita Aponte, MSN

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**Keywords:** Hispanic Nurses, mentoring, career, promotion, retention, military specific

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**Start Date:**  
3/26/2002

**Est. Completion Date:**  
Jul 03

**Periodic Review:**

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**Study Objective:** The purpose of this study is to determine which behaviors or mentoring activities, if any, influence career advancement, promotion opportunities and retention of Hispanic in the Army Nurse Corps. T

**Technical Approach:** A descriptive correlational survey will be used to examine mentoring activities which influence career advancement, promotion, and retention of Hispanic nurses and determine if there is a relationship between mentoring and career advancement, promotion and retention among Hispanic Army nurses in the Army. Data collection will be done using the Alleman Mentoring Scale Questionnaire. This survey will be mailed to all active duty Hispanic Army nurses. Descriptive statistics and multivariate statistics will be used to analyze the quantitative data. It is anticipated that the result of this study will provide a greater understanding of the perceived personal, professional, career development, and socialization patterns of Hispanic nurses in the military. This information could lead to innovative patterns of career development for this minority group in the Federal and Civilian workplace in the future

**Progress:** Currently this multi-center study is on hold pending approval by the WRAMC IRB. Only the survey portion of the protocol will be conducted at MAMC, and todate, no surveys have been received or mailed.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/050                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Health Across the Continuum  |  |                         |
| <b>Principal Investigator:</b> LTC(P) Joann E. Hollandsworth, AN                   |  |                         |
| <b>Department:</b> Nursing   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> Ann K. Lancaster, CHN; Pamela S. Birgenheier, RN |  |                         |
| <b>Keywords:</b> Health education, health promotion in primary care                |  |                         |
| <b>Start Date:</b><br>3/26/2002  | <b>Est. Completion Date:</b><br>Mar 03 | <b>Periodic Review:</b> |

**Study Objective:** This is a quality improvement project to enhance the health education and promotion programs and services within the Primary Care portals. The health education and promotion elements targeted are: tobacco, stress, injury prevention, reproductive health, family violence, alcohol, fitness, safety, and nutrition. Each element will be developed with the following goals: 100% integration between health care delivery and community service agencies. 95% of the Primary Care teams and community service agency staff will receive health education/promotion training on each element. 90% of health education/promotion materials will be standardized. 80% of the Primary Care beneficiary population will receive health education/promotion as part of their clinic visit.

**Technical Approach:** The work plan will utilize the Quality Improvement FOCUSPCDA model. F the process to improve is the fragmentation of health education/promotion within the Ft Lewis/MAMC community as identified by needs assessment; O multidisciplinary QAT teams will be formed for each element; C/U each element will be assessed and ensure that the three levels of prevention are met; S the process to improve is MAMC approach to health education/promotion; P data utilization, resources identification/execution, and intervention strategies developed and instituted; D do the health education/promotion topic of the month to providers (each element will be featured as the topic of the month), begin patient record audits, targeted marketing. Also the project will use a pretest posttest survey format looking at communication, teamwork and readiness to change with in each primary care clinic. The surveys will be one a generic survey and the other will have questions to assess the readiness to change questions for health promotion. The even numbers by last number of their social security will receive the generic survey and the odds will receive the survey with the readiness to change questions. The survey will not contain any identifying information. One of the staff Army Community Health Nurses (ACHN) will go to the clinic during a regular staff meeting and provide and overview of what the survey is being used for and pass out and collect by the end of the staff meeting. ACHN will provide a collection box for the surveys once they are completed

**Progress:** This protocol recently received approval and is in the preparatory stages. No data collection occurred during FY02.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/105 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Care Coordination for Active Duty Soldiers on Profile

**Principal Investigator:** Lori A. Loan, Ph.D.

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** COL Bonnie M. Jennings, AN; Pamela S. Birgenheier, RN; MAJ Gregory A. Marinkovich, MC; Joseph E. Dziados, M.D.

**Keywords:** soldier health care, database development, care coordination

**Start Date:**

8/27/2002

**Est. Completion Date:**

Aug 03

**Periodic Review:**

**Study Objective:** This study will create an infrastructure for improving the care coordination for active duty soldiers by: 1) implementing a process and database to track injured soldiers through the health care system, 2) standardizing practice guidelines to treat soldier musculoskeletal injuries (the most common injury among soldiers), 3) solidifying instruments for use with injured soldiers to test the intervention, and 4) pilot testing an intervention using a nurse care coordinator to facilitate soldiers' moving through the care process. These efforts will provide the foundation for a follow on study to test the ability of nurse care coordination to decrease soldier time on profile and improve soldier, unit, and Army outcomes.

**Technical Approach:** Health care treatment for soldiers is fraught with problems. soldiers express concern about barriers to diagnosis and treatment for injuries. They believe they are not getting optimal post injury care. these barriers to acces result to inclmplete recovery and a delay in return to duty (Jennings & Loan, 2001). Therefore, process changes and an intervention wire designed to facilitate injury recovery and soldier medical profile management. The magnitude of these alterations, however, requires pilot work to guid the development of the infrastructure needed to support examining the intervention (Prescott & Soeken, 1999).Findings from this study have the potential to set the stage for improving care for active duty soldiers and ensuring they are medically ready to deploy.

**Progress:** The study received funding from the TriService Nursing Research Program and is awaiting IRB approval at USUHS. No work has been done on the study.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/066                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Caring Interventions for Couples Who Have Miscarried   |  |                         |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.   |  |                         |
| <b>Department:</b> Nursing   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> Kristen M. Swanson, RN, Ph.D., FAAN; Mark A Biernbaum, Ph.D.; Kathryn Barnard, RN, Ph.D., FAAN; Martha J. Lentz, BSN, MN, Ph.D.; |  |                         |
| <b>Keywords:</b> Miscarriage; healing; couple well-being   |  |                         |
| <b>Start Date:</b><br>5/28/2002  | <b>Est. Completion Date:</b><br>Oct 04 | <b>Periodic Review:</b> |

**Study Objective:** The purpose of this randomized study is to compare the effects of nurse caring (3 nurse counseling sessions), self-caring (3 home-delivered video tapes and journals), combined caring (1 nurse counseling session plus 3 videotapes and journals) and no intervention (control) on the emotional healing, integration of loss and couple well-being of women and their partners (husbands or male mates) in the first year after miscarriage.

**Technical Approach:** 340 couples (or 680 individuals) will be recruited to participate in a 4 group, pre-test, post-test randomized study of a counseling intervention meant to reduce distress and enhance couple well-being following miscarriage. Upon recruitment, individuals will be informed that they may be randomized into a group that will not receive any treatment. Four groups will be followed for 1 year. All participants will fill out 4 questionnaire packets throughout the study period. The first will be mailed after the couple initially agrees to participate. The other questionnaire booklets will be sent at 6 weeks, 16 weeks and 1 year after their initial enrollment in the study.

**Progress:** The study's funding agency, the National Institute for Nursing Research, requires Federal Wide Assurance (FWA) approval. MAMC's FWA was received in mid-September 2002. Training and subject recruitment is expected to begin in November 2002.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/023 | <b>Status:</b> Ongoing |
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**Title:** Correlations Between Coping and Wound Healing in Patients Undergoing Total Knee Arthroplasty

**Principal Investigator:** Lori A. Loan, Ph.D.

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| <b>Department:</b> Nursing | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** Ann M. Gaspari, RN, BS

**Keywords:** coping, wound healing

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| <b>Start Date:</b><br>1/22/2002 | <b>Est. Completion Date:</b><br>Jun 02 | <b>Periodic Review:</b> |
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**Study Objective:** The specific aims of this study are to explore relationships between coping processes (as measured by the Ways of Coping questionnaire), surgical wound healing (as measured by hydroxyproline accumulation) and total knee arthroplasty wound complications (as measured by the ASEPSIS instrument) within and between the preoperative and postoperative periods.

**Technical Approach:** This study is a descriptive, correlational secondary analysis of a subset of patients from a larger investigation conducted at Madigan Army Medical Center titled "Effects of stress response on wound healing" (MAMC PI- Dr. Lori A. Loan). Data obtained for this study will be recorded such that subjects cannot be identified directly or by identifiers linked to the subjects. Methods of analysis will include descriptive statistics and correlations among the Ways of Coping Questionnaire data, the hydroxyproline data, and the wound complication data. First, indicators of coping wound healing and wound complications will be reported as mean scores or as a percentage of the sample. Second, the relationship within the preoperative and postoperative indicators will be determined using a Pearson's or Spearman's correlation, depending on the distribution of the values. Then, the preoperative indicators will be correlated with the postoperative indicators. The level of acceptable significance will be set at  $p < .05$ . The overall pattern of relationships will be described. Inconsistent findings, even if significant at  $p < .05$ , will be considered suspect and interpreted cautiously.

**Progress:** Secondary analysis of 53 data from patients enrolled in the original study is complete and show: (1) a change in some of the coping strategies used by subjects when comparing pre and post operative coping methods; and (2) three relationships between coping strategy and wound healing--use of positive appraisal preoperatively was positively associated with hydroxyproline accumulation ( $r = .38$ ,  $p = .03$ ), preoperative use of "accepting responsibility" was negatively related to histologic presence of loose connective tissue ( $r = -.35$ ,  $p < .03$ ), and postoperatively the use of "planful problem solving" was negatively related to hydroxyproline amount ( $r = -.36$ ,  $p = .05$ ).

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/101                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Establishing a Military Nursing Outcomes Database             |  |                         |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.                          |  |                         |
| <b>Department:</b> Nursing  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> LTC Laura R. Brosch, AN;                  |  |                         |
| <b>Keywords:</b> patient safety, staffing effectiveness, outcome management |  |                         |
| <b>Start Date:</b><br>8/27/2002   | <b>Est. Completion Date:</b><br>Dec 03 | <b>Periodic Review:</b> |

**Study Objective:** To create and implement a high quality database consisting of data related to nurse staffing effectiveness and patient safety indicators. This current proposal represents Stage Three of the nursing relevant database research program. The aim of this stage is to expand and sustain a high quality military patient safety and nurse staffing effectiveness database

**Technical Approach:** The global aim of this long term, multi-staged military nursing research program is to create and implement a high quality database consisting of data related to nurse staffing effectiveness and patient safety indicators. This data could then be used to support evidence-based clinical and administrative decision-making, as well as research, in the Department of Defense. This current proposal represents Stage Three of the research program. The aim of this stage is to expand the Military Nursing Outcomes Database (MiNOD) to seven MTFs- four Army, two Navy and one Air Force and sustain the collection of high quality military patient safety and nurse staffing effectiveness data for a six month period. Analysis will include a variety of techniques and consist of examination of data elements and collection processes for reliability and validity.

**Progress:** Study funding was received in late August 2002; a project director was hired in September 2002, and work was begun to identify site coordinators and obtain IRB approvals at all seven sites.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/095 | <b>Status:</b> Ongoing |
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**Title:** Expectations of Military Health Care: An Inductive Analysis

**Principal Investigator:** Lori A. Loan, Ph.D.

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| <b>Department:</b> Nursing | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL Bonnie M. Jennings, AN; Debra DePaul, RN; COL Eileen A. Hemman, AN; LTC Julie Fitch, AN

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**Keywords:** TRICARE, military health care, health care expectations, health care experiences, military specific

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**Start Date:**

6/27/2000

**Est. Completion Date:**

Jun 02

**Periodic Review:**

7/23/2002

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**Study Objective:** To acquire empirical evidence for use in reforming military health care, for the purpose of improving patient satisfaction and quality.

**Technical Approach:** Focus groups consisting of active duty personnel and family members of active duty personnel, will be utilized in this study to present customer satisfaction/expectation questionnaires to recipients of military medical care and use the results to analyze both real and perceived strengths and weakness of the Military Health System. Focus groups specific to health care personnel will also be conducted to explore differences between consumer expectations and health care personnel perceptions of the care delivery process.

**Progress:** Twelve focus groups have been conducted, seven at Ft. Bragg and the surrounding area, and five at Ft. Lewis and the surrounding area. Analysis for the first cluster of focus groups is finished. The second cluster of focus groups consisting of TRICARE remote beneficiaries is complete. Data analysis for this cluster is in progress.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   |  | <b>Number:</b> 99/028                  |  | <b>Status:</b> Completed              |  |
| <b>Title:</b> Factors Associated with Preventable Hospitalization in Older Military Retirees   |  |  |  |                                       |  |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.   |  |  |  |                                       |  |
| <b>Department:</b> Nursing   |  |  |  | <b>Facility:</b> MAMC                 |  |
| <b>Associate Investigator(s):</b> COL Bonnie M. Jennings, AN; Ms Suzanne K. Wilson, MSN, RN; LTC Laura R. Brosch, AN; Rebecca S. Miltner, RNC, MS  |  |  |  |                                       |  |
| <b>Keywords:</b> Hospitalization, military retirees, military health care system   |  |  |  |                                       |  |
| <b>Start Date:</b><br>2/23/1999  |  | <b>Est. Completion Date:</b><br>Jun 01 |  | <b>Periodic Review:</b><br>12/18/2001 |  |
| <b>Study Objective:</b> To prospectively assess the relationship between patient-specific characteristics and the likelihood of preventable hospitalization for Tricare Senior Prime enrollees.  |  |  |  |                                       |  |
| <b>Technical Approach:</b> All 3,620 Madigan Army Medical Center Tricare Senior Prime enrollees will be surveyed to obtain baseline predisposing (age, gender, race, education, living arrangements), enabling (income, tangible social support, perceptions of regular source of care, transportation, transportation time) and need factor (perceived physical health status, perceived mental health status, perceived functional limitations, chronic illnesses, past hospital use) data. These data will subsequently be linked to hospitalization data prospectively collected for the 12 month period following the survey. Each study participant's hospital use will be classified into one of three categories: (1) no hospital admissions, (2) at least one potentially preventable hospitalization, or (3) hospitalized, but not for a potentially preventable condition. Descriptive statistics will be used to profile the sample in terms of the factors under study and summarize the frequency of occurrence of each type of hospital use. Multivariate polytomous logistic regression will be used to identify predisposing, enabling and need factors associated with the likelihood of potentially preventable hospitalization.  |  |  |  |                                       |  |
| <b>Progress:</b> All data collection for this study occurred during FY01. The sample included 3,620 MAMC TSP enrollees. Only need factors were found to be associated with an increased risk of preventable hospitalizations in this military population. TSP enrollees with lower SF-36 PCS scores, 2 or more ADL needs, a reported history of emphysema, acute MI, or heart disease, or a past hospitalization in the last 12 months were more likely to experience a preventable hospitalization. Patients with a history of emphysema or heart disease were more likely to be hospitalized for a preventable condition than hospitalized for another medical condition. Patients with a history of cancer were less likely to be hospitalized for a preventable condition than hospitalized for another condition. These findings support Andersen's Model of Health Services Use and suggest that access to care was equitable for MAMC TSP enrollees. Findings generated the following recommendation--upon enrollment, seniors should complete comprehensive self-assessments. These data should be used to identify patients at risk for preventable hospitalization. In addition, enrollment in specialized ambulatory care health promotion or disease management programs may be of benefit to specific subpopulations of military seniors at greatest risk for preventable hospitalization. Future research aimed at reducing preventable hospitalizations may need to target how individuals with specific chronic medical problems obtain ambulatory care. |  |  |  |                                       |  |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/053 | <b>Status:</b> Ongoing |
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**Title:** Improving Soldier Access to Urinary Incontinence Therapy

**Principal Investigator:** Lori A. Loan, Ph.D.

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**Department:** Nursing

**Facility:** MAMC

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**Associate Investigator(s):** LTC Ann M. V. Bianchi, AN; LTC (Ret) Richard A. Sherman, Ph.D.; MAJ Carol F. Halle, AN

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**Keywords:** Urinary incontinence, female soldiers, Kegels, military specific

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**Start Date:**

1/16/1998

**Est. Completion Date:**

Sep 98

**Periodic Review:**

11/27/2001

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**Study Objective:** This study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for exercise-induced urinary incontinence in the troop medical clinic environment with those receiving similar treatments at a medical center.

**Technical Approach:** All subjects interested in participating in the study will be screened for evaluation of the lower urinary tract. If inclusion criteria is met, the subject will be randomized to treatment at either the TMC or MAMC and be scheduled for treatment visits every 2 weeks for 12 weeks. During the first visit, demographic and descriptive information will be gathered and subjects will learn how to do Kegel exercises using biofeedback. Subjects will be asked to keep daily logs and to practice the Kegel exercises for twenty minutes two times a day. Subsequent visits to the treatment center will be to encourage continuation and the keeping of daily logs. At the final visit more demographic and descriptive information will be asked and a Patient Satisfaction Questionnaire will be filled out by each subject. The portable biofeedback equipment will be used to evaluate Kegel performance during this final visit.

**Progress:** During FY02 screening tools were mailed to 1,017 female soldiers newly assigned to the Ft. Lewis area. Survey respondents indicating a desire for the study intervention will be screened and if eligible recruited to participate in one of two groups in this study or a third group in a study called "In-Home Urinary Incontinence Therapy for Female Soldiers." A total of 102 patients have been enrolled in this study at MAMC, with 22 patients enrolled during FY02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 98/044                  | <b>Status:</b> Ongoing                |
| <b>Title:</b> Physical Activity and Exercise in AD Female Soldiers               |  |                                       |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.                               |  |                                       |
| <b>Department:</b> Nursing   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> Debra DePaul, RN; LTC Laura R. Brosch, AN;     |  |                                       |
| <b>Keywords:</b> Physical activity, exercise, female soldiers, military specific |  |                                       |
| <b>Start Date:</b><br>2/20/1998  | <b>Est. Completion Date:</b><br>Oct 98 | <b>Periodic Review:</b><br>12/18/2001 |

**Study Objective:** To examine the physical activity levels and habitual exercise patterns of active duty female soldiers and to identify factors that influence those habits in hopes of producing information to be used to improve the health of female soldiers.

**Technical Approach:** Each subject will complete an initial survey and APFT scores will be obtained for each service member consenting to be in the study. Focus groups will then explore the issues among subjects identified as belonging to subgroups at risk for low exercise participation.

**Progress:** Of the 2623 female soldiers responding to the survey, nearly 40% reported an injury from exercise and two thirds exercised less than five times per week. Nutrition, injury, perceived benefits associated with exercise, social support for exercise, self-efficacy for exercise and living with a spouse predicted 40% of the variance in habitual exercise. Purposive sampling techniques were utilized to identify survey respondents who, by self-report, had an injury from exercise and/or an injury profile, to participant in focus groups. Participants related their and other female soldiers experiences with injuries and health care following injury, suggested ways to create variety during physical training, and provided suggestions for preventing exercise-related injuries. Participants frequently cited pressure to perform during physical training, fear about falling out from formation runs, lack of ability groups as part of the physical training, and the stigma created by an injury profile especially for female soldiers. Findings from the study will serve as a basis for the development and testing of interventions targeted at injury prevention for female soldiers, support for their recovery from injuries, and their return to fitness.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 200/047      **Status:** Ongoing

**Title:** Prone Position and the Pattern of Oxygenation in Acute Lung Injury Patients

**Principal Investigator:** Lori A. Loan, Ph.D.

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** COL Janet R. Harris, AN; Mary S. McCarthy, RN, MNS; LTC George N. Giacoppe Jr., MC; Kathleen Vollman, RN

**Keywords:** prone position, oxygenation, acute lung injury, ALI, adult respiratory distress syndrome

**Start Date:**

3/28/2000

**Est. Completion Date:**

Dec 03

**Periodic Review:**

5/28/2002

**Study Objective:** To examine the pattern of oxygenation in 60 patients with acute lung injury (ALI)/adult respiratory distress syndrome (ARDS) who undergo a 4-hour prone positioning trial and to develop evidence-based guidelines for a prone positioning protocol regarding safety, timing, and frequency of the intervention for patients with ALI or ARDS.

**Technical Approach:** Informed consent will be obtained from the patient or surrogate prior to participation in the study. Patient ventilator settings, positive end-expiratory pressure (PEEP) and inspired oxygen fraction (FiO<sub>2</sub>), will be established by the patient's physician according to the clinical needs of the patient. During the data collection periods for this study, the ventilator settings will remain unchanged. An Acute Lung Injury Score (Murray et al., 1988) will be assessed for each subject to further delineate the severity of acute pulmonary damage. Prior to data collection all equipment will be calibrated according to the manufacturer's recommendations. The arterial line will be calibrated and leveled to the subject's phlebostatic axis (Boggs & Wooldridge - King, 1993). Baseline supine measurements will occur after the subject has been in the supine position for at least one hour and just prior to turning the subject to the prone position. Following site visits to both facilities by the Consultant who is the developer and an expert in the device to be used for the intervention, trained teams will be identified. The subject will be turned to the prone position. PaO<sub>2</sub>/FiO<sub>2</sub> will be measured every hour for the 4 hours the subject is in the prone position. The subject will remain in the prone position for 4 hours unless the subject does not tolerate the prone position or has an emergency (loss of airway or central access, cardiopulmonary resuscitation, hemodynamic instability). Following initial measurements in the baseline supine position, measurements will be conducted at 1 hour intervals while the subject is in the prone position and 1 & 2 hours after returning to the supine position.

Subject demographics that will be collected include: age, gender, diagnoses, etiology of acute lung injury, parenteral and enteral nutrition, date of admission to ICU, duration of time since first diagnosed with ALI, days of mechanical ventilation before initial prone trial, Acute Lung Injury Score, and severity of illness as measured by the APACHE II scoring tool.

**Progress:** No patients enrolled on this study during FY02. This study continues to have great difficulty recruiting subjects. The Project Director attends ICU rounds several times a week looking for appropriate candidates for prone positioning. MDs are reluctant to subject critically ill mechanically ventilated patients to such extreme positioning. There have also been long periods of time with no suitable candidates as criteria for inclusion is very selective. Brooke AMC has been added to the protocol as a recruitment site and Wright -Patterson AFB is awaiting IRB approval for their participation in the study. The consultant for this study, an expert in prone positioning, will return soon for education of new medical and nursing staff.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/075                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Secondary Analysis of NICU Modified Care Environment Projects   |  |                         |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.  |  |                         |
| <b>Department:</b> Nursing  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> Karen A. Thomas, Ph.D., RN; Susan T. Blackburn, Ph.D., RN, FAAN; Shu-Yuann Wang, MS, RN; Sara Brown, RN; Shao-Yu Tsai |  |                         |
| <b>Keywords:</b> Infants caregiving nursing sleep outcomes  |  |                         |
| <b>Start Date:</b><br>6/25/2002   | <b>Est. Completion Date:</b><br>May 05 | <b>Periodic Review:</b> |

**Study Objective:** Secondary analysis of data collected in previously approved projects is proposed. Prior human use approvals were (1) The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants, P.I. LTC Michelle T. Renaud, approved 4 September 1992, and (2) a continuation and extension, Neonatal Outcomes in a Modified NICU Environment, P.I. LTC Michelle T. Renoud, approved 13 July 1993. Additionally these projects were approved by the University Of Washington Human Subjects Division. Both projects included Karen Thomas and Susan Blackburn, UW faculty, as Co-Principal Investigators. The original projects involved comparison of two neonatal intensive care unit environment that included reduced light and sound levels. Infants randomized to the control group remained in the standard nursery. Both groups of infants received standard medical and nursing care in all respects, except for the nursery environment. Data collected during the study included infant health status, parent demographic information, duration of hospitalization, environmental sound and light levels, neurologic and behavioral assessment and infant sleep-wake states. Infant sleep-wake states were measured by 3-4 hour video recordings performed at 34 weeks gestational age and again at time of discharge. Video recordings were performed while infants were in incubators or in open crib and display the infant's body and face. For the second analysis, investigators are requesting permission for activities: (1) Photo copies to be made of existing video coding sheets, (2) Access to video tapes for recording purposes, (3) Use of existing data base by the three graduates named above.

**Technical Approach:** The proposed research is a secondary analysis of data from a previously approved project that was conducted at MAMC in conjunction with nurse researchers from the University of Washington Department of Family and Child Nursing. Permission is requested for use of data by a total of three nursing graduate students. Computer files containing the data from the original project, excluding identifiers, is currently in the possession of Karen Thomas. Permission is requested to photocopy the video coding sheets, currently held at MAMC for use by investigators at the University of Washington. Permission is also requested for temporary use of the videotapes at the U.W. The video coding sheets will be used to enter the raw data into a computer file. Videos will be used to determine reliability of original coding and to code additional infant behaviors and caregiving activities.

**Progress:** Two graduate nursing students have entered coded video tape data from 42 subjects in the original study into computer files. Data analysis is currently in process. The analysis will focus on the relationship between infant state and caregiving activities. These two thesis projects are scheduled for completion in June, 2003. One University of Washington nursing doctoral student is currently reviewing the 333 videotapes, developing coding strategy and analysis plans to examine the effect of swaddling on infant state.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/011      **Status:** Ongoing

**Title:** The Effects of Postoperative Supplemental Oxygen on Tissue and Wound Healing

**Principal Investigator:** Lori A. Loan, Ph.D.

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** Kathleen A. Clary, RN; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Jerome B. Myers, MC; MAJ Jeannie M. Muir-Padilla, MC; JoAnne D. Whitney, Ph.D., RN

**Keywords:** Oxygen, Wound healing, Nursing, Urology, subcutaneous tissue oxygen tension

**Start Date:**

11/28/2000

**Est. Completion Date:**

Oct 01

**Periodic Review:**

10/31/2002

**Study Objective:** The specific aims of this study are to: (1) Compare the effects of 36 hours of supplemental oxygen therapy provided postoperatively to patients having cystectomy and nephrectomy surgery, to management without supplemental oxygen on: (a) wound healing in test wound tissue samples obtained on the 7th postoperative day including: (1.) hydroxyproline accumulation determined by high performance liquid chromatography; and (2.) mRNA for Pro  $\alpha$  1(I) collagen as measured by in situ hybridization (3.) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation and (b) subcutaneous tissue oxygen tension (PscO<sub>2</sub>) in test wound sites on postoperative days 0, 1 and 2 using a subcutaneous tonometer/electrode system. (2) Compare the incidence of wound complications between the two groups evaluated in the surgical wound on the 2nd and on the 7th postoperative day using a wound registry scoring tool. (3) Compare clinical healing outcomes (satisfactory/not satisfactory), and describe complications that occurred in the two groups during the 30 days post surgery.

**Technical Approach:** The study utilizes a randomized, two group, experimental repeated measures design. Eight subjects with a need for cystectomy and nephrectomy surgery, ages 18 and above, will be recruited for the study. Subjects will be randomly assigned to receive only room air (control group) or supplemental oxygen at 28% via nasal cannula (n/c) for 36 hours postoperatively (treatment group). PscO<sub>2</sub> will be measured at Hour 1, 18, and 36 using a tonometer/sensor system. Wound healing is evaluated by analysis of tissue cellularity and hydroxyproline from a tissue sample obtained from a small, polytetrafluoroethylene tube placed subcutaneously and removed on the 7th postoperative day. Wound complications/infections will be evaluated using the Wound Registry. Differences between groups will be tested using Analysis of Variance for repeated measures, Wilcoxon Rank Sum test, and Chi-square.

**Progress:** Subject recruitment has been on hold pending IRB approval of a revision to the protocol. Specifically, the intervention was changed from 36 hours of supplemental oxygen to 24 hours. This change was based on the decreasing length of potential subject's hospital stay, and growing evidence that interventions to prevent wound complications are most beneficial when timed close to the surgical procedure (Greif et al, 2000). Subject recruitment will resume as soon as University of Washington IRB approval has been received.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/070                 | <b>Status:</b> Ongoing              |
| <b>Title:</b> The Use of Body Fat Analysis and Severity of Illness to Determine Energy Expenditure in the Obese Critically Ill Patient |  |                                     |
| <b>Principal Investigator:</b> Lori A. Loan, Ph.D.   |  |                                     |
| <b>Department:</b> Nursing   | <b>Facility:</b> MAMC                  |                                     |
| <b>Associate Investigator(s):</b> Mary S. McCarthy, RN, MNS; Janet C. Fabling, RD, CNSD  |  |                                     |
| <b>Keywords:</b> Obesity, nutritional assessment, metabolism, energy expenditure, ICU, critical issues, mechanical ventilation         |  |                                     |
| <b>Start Date:</b><br>2/27/2001  | <b>Est. Completion Date:</b><br>Dec 02 | <b>Periodic Review:</b><br>1/8/2002 |

**Study Objective:** The specific objectives of this study are: (1) to formulate a predictive equation for energy expenditure (EE) to be used in the nutritional assessment of the obese, critically ill patient, (2) to utilize a state-of-the-art, portable, body composition analyzer to measure body fat for inclusion into the equation, (3) to document APACHE II scores for inclusion into the equation, and (4) to perform indirect calorimetry on all study patients to obtain the measured resting energy expenditure (MREE).

**Technical Approach:** This study is intended to evaluate the benefit of percent body fat and severity of disease to a predictive equation of energy expenditure in the obese, critically ill patient. The study involves the collection of patient data during routine nutritional assessment. A predictive correlational design will be used to derive a regression equation that is + 10% of measured resting energy expenditure obtained via indirect calorimetry. A convenience sample of the first 70 adult ICU patients who meet the National Heart, Lung, and Blood Institute criteria for overweight (BMI 25.0 - 29.9 kg/m<sup>2</sup>) and obesity (>30.0 kg/m<sup>2</sup>) will be used for data collection. It is anticipated that enrollment will take about 18 months. The associate investigator, a registered dietitian with duties in the ICU, will identify subjects during their routine admission nutritional assessment. The PI makes rounds regularly with the ICU team and she too will identify candidates for the study. The PI will perform body fat analysis and indirect calorimetry on two separate occasions. Chart review will provide the data for APACHE II score and the other equation predictors of age, gender, actual weight, and ventilatory status. A regression equation will be derived using multivariate correlation analyses. The equation will correlate within + 10% of the measured resting energy expenditure to be considered acceptable in this population.

**Progress:** A total of 13 patients have been enrolled into this study during FY02. Protocol progress is slow but steady. The limiting factor for recruitment has been that many patients have ventilator settings that preclude use of the metabolic cart. Also, supplies have been difficult to obtain for the cart due to a lack of funds in the Respiratory Care Service. It is anticipated that the study will achieve its goal of 75 subjects over the next 6-12 months.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/075 | <b>Status:</b> Ongoing |
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**Title:** E-Health Management of Fibromyalgia Pain (VPCC Substudy)

**Principal Investigator:** LTC Fujio McPherson, AN

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** LTC Gregory A. Gahm, MS; Deland Peterson, Ph.D.; Jon C. Allison, M.D.

**Keywords:** E-Health, Primary Care, Nursing, Fibromyalgia, Pain, Psychology, Telemedicine, Health Promotion

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**Start Date:**

3/27/2001

**Est. Completion Date:**

May 01

**Periodic Review:**

2/6/2002

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**Study Objective:** (1) Evaluate the effects of using regular electronic communication that includes content information about specific patient health concerns, cognitive behavioral therapy, medication, exercise, lifestyle changes, complimentary/non-traditional health care and health promotion information via the internet, in the treatment of patients with fibromyalgia, (2) Evaluate the workload requirements and appropriateness of having primary care providers working in collaboration with a clinical psychologist to implement supportive psychotherapy into this process, and (3) Identify the use of complimentary/non-traditional medical practices among patients with fibromyalgia and their impact on patient outcomes.

**Technical Approach:** The study will involve a random assignment of patients with a diagnosis of fibromyalgia/myalgia. An enrollment questionnaire will then be forwarded to them which provides inclusion and exclusion criteria. Those who meet the inclusion criteria and agree to be included in the study will be divided into two groups. The first group (experimental group) will be subject to the interventions designed in the study (being provided information and access to the VPCC via the internet), the second group (control group) will continue to receive care thorough the primary care portal without access to e-health. Although the control group will not be restricted from using their Internet servers to access non-VPCC sources of information. The experimental group will then be given a group presentation to instruct them on the study parameters, specifically how to access the VPCC system using their Internet interfaces. From that time until the conclusion of the study, information will be provided electronically to and from the experimental group using the VPCC. The control group, minus the Internet briefing will receive the same questionnaire via routine postal service. Retrospective and prospective data will be collected from both groups prior to the study, three months after the study and at the conclusion of the study, projected at six months.

**Progress:** A total of 15 patients have been enrolled in the study at MAMC during FY02. Data analysis has begun.

### Detail Summary Sheet

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|--|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/045                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> Determining the Need for a Bereavement Program at a Military Medical Center  |  |                                       |
| <b>Principal Investigator:</b> LTC Elizabeth A. Mittelstaedt, AN   |  |                                       |
| <b>Department:</b> Nursing   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> LTC Wynona M. Bice-Stephens, AN; CPT Carie G. Bussey, AN; Kathi M. Hamilton, DAC   |  |                                       |
| <b>Keywords:</b> grief, bereavement, support, death, counseling, dying, education, staff education   |  |                                       |
| <b>Start Date:</b><br>2/27/2001  | <b>Est. Completion Date:</b><br>Jan 02 | <b>Periodic Review:</b><br>12/10/2001 |
| <b>Study Objective:</b> To determine the level of MAMC nursing staff knowledge regarding patient death, dying and grief.   |  |                                       |
| <b>Technical Approach:</b> The study will occur at Madigan Army Medical Center. Potential participants will include nursing staff members. The survey will include demographic questions and a self-assessment regarding grief, death, and dying. The survey will also address information about current facility activities regarding death and dying. The survey is voluntary, and distributed to each individual in person or via their unit mailboxes/Head Nurse. The surveys will be distributed and collected within a 14-day timeframe. Social security numbers, addresses or other identifying data will not be requested. Descriptive statistics will be applied to quantitative and demographic data; qualitative data will be categorized. The responses to this survey will provide invaluable information regarding current aspects of grief support at the Medical Center. Respondents will also provide key information regarding their grief support needs. The implications of this study will assist the Hospital Bereavement Committee to develop educational programs, support systems and services to meet the needs of staff, students, and patients at Madigan Army Medical Center. |  |                                       |
| <b>Progress:</b> Analysis was started on the results of this study, but no work has been done for approximately 8 months due to time constraints. No data analysis is available at this time.  |  |                                       |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/077 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** The Relationship Between Health Locus of Control, Self-Care Agency, Health Promoting Behaviors and Glycemic Control in Adults with Type 2 Diabetes and Internet Use: A Randomized, Controlled Trial (VPCC Substudy)

**Principal Investigator:** LTC Mary A. Schwenka, AN

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|----------------------------|-----------------------|
| <b>Department:</b> Nursing | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Nhan V. Do, MC; LTC Gregory A. Gahm, MS

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**Keywords:** Type 2 Diabetes, glycemic control, Internet, Health locus of Control, Self-care Agency, health promotion, patient education.

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**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
2/15/2002

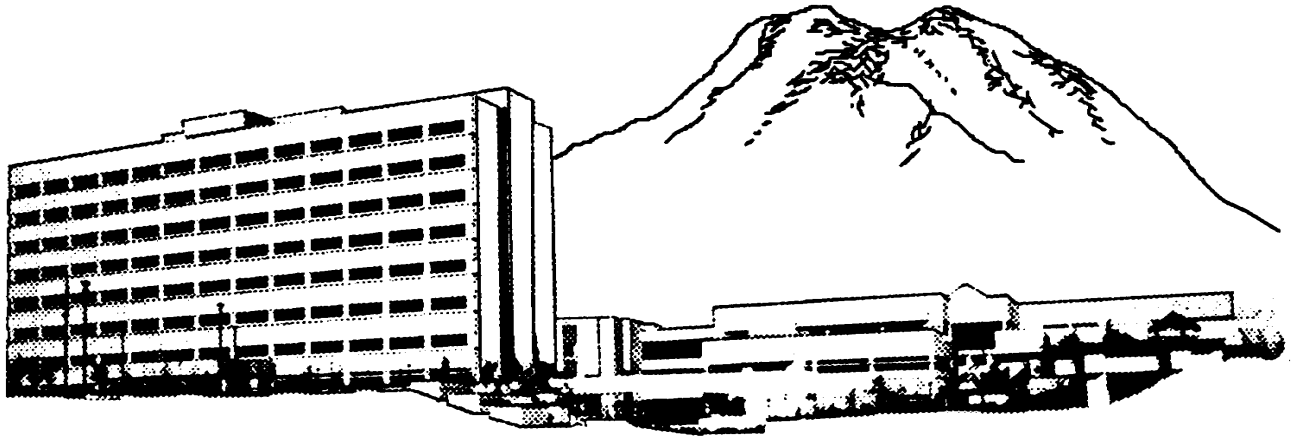
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**Study Objective:** Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patient with Type 2 Diabetes using Internet technology and that integrating Internet Healthcare tools with traditional clinical practice can improve Health Promoting Behaviors, Health Locus of Control, and Self-Care Agency scores in patients with Type 2 Diabetes.

**Technical Approach:** Our study population will include both male and female patients from the APCC Cascade team with diabetes but without advanced or severe complications from diabetes and age range from 18 to 75. Study design is a randomized non-blinded descriptive correlational study. The providers on the Cascade team will manage both the control and study group. Patients in the study group will have their diabetes managed the traditional method which includes routine office visit and phone calls. The study group will be managed with routine office visit but with electronic communications and a limited computer clinical support system. The primary endpoint is the change in hgbA1c from baseline. Secondary endpoints will include scores from Health Locus of Control, Self-Care Agency, and Health Promoting Behaviors instruments, patient and provider's satisfaction, and clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and scoring of instruments per published protocols.

**Progress:** A total of 15 patients have been enrolled in this study, which is currently in its second week. Study will complete and data analysis will begin in FY03





## **Detail Summary Sheets**

### **Anesthesia Students, Department of Nursing**

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/006 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

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**Title:** Postoperative Pain Following PSOAS Compartment Block with General Anesthesia as Compared to Subarachnoid Block for Total Knee Arthroplasty

**Principal Investigator:** CPT Jamie P. Cherry, AN

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**Department:** Nursing/Anesthesia

**Facility:** MAMC

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**Associate Investigator(s):** CPT Faye H. Wilson, AN; LTC Elizabeth E. Hill, AN; MAJ James A. Hall, MC; Mark D. Hachey, CRNA

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**Keywords:** Postoperative Pain, Psoas, Compartment Block General Anesthesia, Subarachnoid Block, Total Knee Arthroplasty

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**Start Date:**  
10/23/2001

**Est. Completion Date:**  
Nov 02

**Periodic Review:**

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**Study Objective:** The purpose of this study is to compare the effectiveness of the Psoas Compartment Block (PCB) combined with general anesthesia versus the Subarachnoid Block (SAB) alone in controlling postoperative pain in patients undergoing a total knee arthroplasty (TKA).

**Technical Approach:** This study will enroll a convenience sample of 56 patients with an ASA I, II, and III, who are undergoing a TKA at MAMC. Patients will be recruited from the orthopedic clinic and the Surgical Services Clinic (SSC). Consented patients will be randomly assigned to groups receiving either PCB with general anesthesia or SAB without general anesthesia. Postoperative pain will be measured using visual analogue scale (VAS) scores and amount of postoperative opioids administered via a patient controlled analgesia (PCA) pump. Scores on the VAS and milligrams of opioids administered via PCA will be measured prior to leaving the Post Anesthesia Care Unit (PACU) and at 8, sixteen and twenty-four hours postoperatively. Repeated measures analysis of variance will be used to compare scores on the VAS and to compare use of postoperative opioids at these data points. Nurses in the PACU and on the orthopedic ward will receive an inservice related to the study, and will conduct all data collection.

**Progress:** This study was reported as completed prior to obtaining the computed sample size due to time constraints of the academic anesthesia nursing program. Nine patients enrolled in this study at MAMC. No adverse events were reported. Data collected is to be analyzed as a pilot study. An abstract is not yet available.

### Detail Summary Sheet

|   |  |                          |
|---|--|--------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/007                 | <b>Status:</b> Completed |
| <b>Title:</b> Intravenous Cosyntropin Therapy vs Epidural Blood Patch in the Treatment of Post Dural Puncture Headache  |  |                          |
| <b>Principal Investigator:</b> CPT Leland B. Morgans, AN  |  |                          |
| <b>Department:</b> Nursing/Anesthesia   | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> CPT John Murphy, AN; CPT Charles Trudo, AN; LTC Elizabeth E. Hill, AN; MAJ James Aylor, AN; LTC Stephen L. Bolt, MC   |  |                          |
| <b>Keywords:</b> post dural puncture headache, PDPH, Cosyntropin, dural puncture, epidural blood patch, ACTH, adrenocoritotropic hormone  |  |                          |
| <b>Start Date:</b><br>10/23/2001  | <b>Est. Completion Date:</b><br>Aug 02 | <b>Periodic Review:</b>  |
| <b>Study Objective:</b> To compare the effectiveness of Intravenous Cosyntropin therapy, 15micrograms per kilogram (mcg/kg), with the epidural blood patch for the treatment of post dural puncture headache.   |  |                          |
| <b>Technical Approach:</b> After informed consent and random assignment have been obtained, subjects in the epidural blood patch group (EBP) will receive the epidural blood patch as prescribed by Madigan Army Medical Center protocol. The intravenous cosyntropin therapy group will receive cosyntropin, 15 micrograms per kilogram infused over 30 minutes. Patients will be evaluated with the Short Form-McGill Pain Questionnaire (SF-MPQ) and the Visual Analog Scale (VAS) at four time periods. These periods are prior to treatment, 30 minutes post treatment, two hours post treatment and twenty-four hours post treatment. The patient will be required to stay at the facility until the two hour assessment is completed after which the patient may go home. The patient will receive a self-addressed stamped envelope and instructions for completing the SF-MPQ and VAS at the twenty four hour period. The patient will be telephoned at home by a member of the study to remind them to fill out the paperwork. Data will be analyzed comparing the effectiveness of Cosyntropin to EBP pretreatment and three times post therapy to see if there is a difference between the two study groups. A two-way mixed ANOVA will be used to evaluate the data. |  |                          |
| <b>Progress:</b> This study was reported as completed prior to obtaining the computed sample size due to time constraints of the academic anesthesia nursing program. Eight patients enrolled in this study at MAMC; however, two were withdrawn as a result of the IV cosyntropin not being effective at the two hour measurement and patients opting to receive blood patch. An abstract is not yet available.  |  |                          |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/119 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Comparison Of Gender Differences In Perceived Pain Following Preemptive Ketamine In Patients Undergoing Selected Ear, Nose, and Throat Surgery

**Principal Investigator:** CPT Dennis R. Turner, AN

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**Department:** Nursing/Anesthesia

**Facility:** MAMC

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**Associate Investigator(s):** CPT Robert N. Ladd, AN; 1LT Carrie L. Pike, AN; COL Eileen A. Hemman, AN; MAJ James Aylor, AN; CPT Brian Baumgartner, MC; Allyson A. Peterson, RN

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**Keywords:** General Anesthesia Postoperative Pain Preemptive Analgesia Gender Difference Ketamine

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**Start Date:**  
9/24/2002

**Est. Completion Date:**  
Apr 03

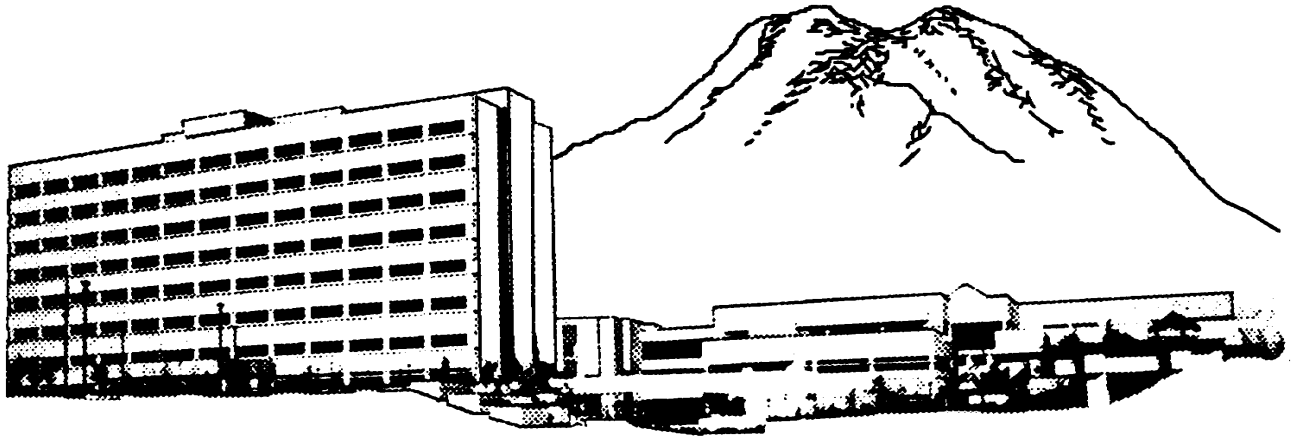
**Periodic Review:**

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**Study Objective:** The purpose of this study is to compare the gender differences in perceived pain following preemptive ketamine in patients undergoing selected ear, nose, and throat surgery.

**Technical Approach:** Patients will be recruited by the investigators from the ear, nose and throat clinic and the Surgical Services Clinic at MAMC. Subjects will be randomly stratified to treatment or placebo groups using a table of random numbers. The study drug will be given by the anesthesia provider after the subject has been induced for anesthesia and prior to the first surgical incision. Postoperative pain will be measured using the NRS. Pain scores, total postoperative analgesic consumption and TFA will be collected in the postoperative period. Pain scores will be collected on arrival to the PACU and at the 1st, 4th, 12th and 24th hour following surgery. Subjects who are discharged before the 24 hour data collection period will be asked to complete a pain survey and record pain scores at the specified data points while at home. Total number of analgesics taken while at home within the 24 hour period will also be recorded on the questionnaire. The investigators will follow up by telephone on the first postoperative day to evaluate the subject's perioperative experience and assist with the questionnaire if necessary. At that time, the investigator will ask about and record the subject's pain scores at the 12th and 24th hours and the total number of analgesics consumed while at home. Data will be analyzed using SPSS® software. The Friedman Test will be used to determine the gender differences between the scores on the NRS. ANOVA will be used to determine the gender differences between the total amounts of opioids received postoperatively and time from completion of surgery to patient's first request for pain medication.

**Progress:** This study recently received IRB approval and has not yet been initiated at MAMC.



## **Detail Summary Sheets**

### **Nutrition Care Division**

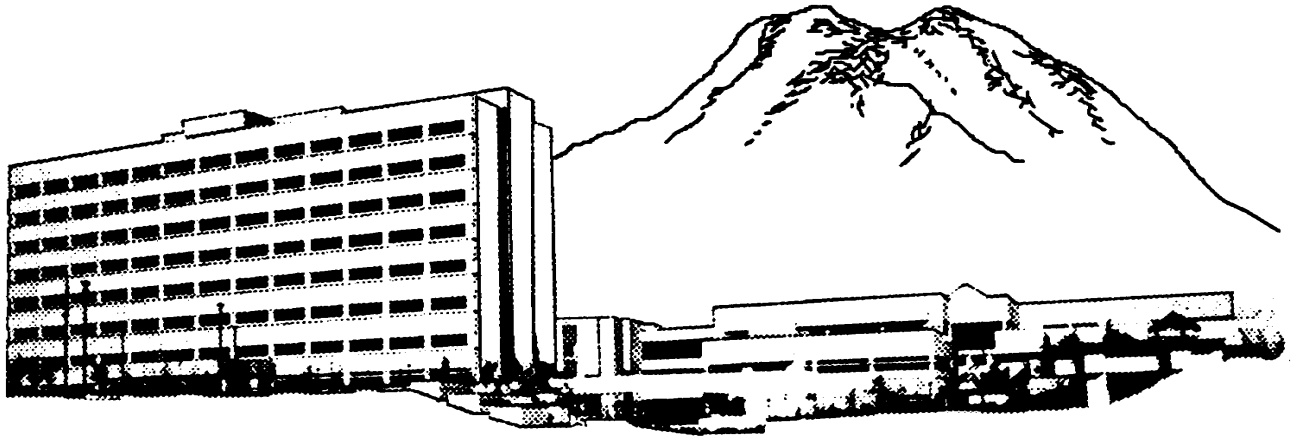
### Detail Summary Sheet

|  |  |                                      |
|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/132                 | <b>Status:</b> Completed             |
| <b>Title:</b> Army Weight Control Program - Identifying Predictors of Success          |  |                                      |
| <b>Principal Investigator:</b> CPT Michelle D'Amico, SP                                |  |                                      |
| <b>Department:</b> Nutrition Care  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b>  |  |                                      |
| <b>Keywords:</b> weight control, active duty weight control program, military specific |  |                                      |
| <b>Start Date:</b><br>9/26/2000  | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>7/16/2002 |

**Study Objective:** The aims of this study are to (1) identify factors that predict the ability of Active Duty soldiers in the AWCP to successfully achieve the standards and (2) specifically, identify the motivators, attitudes and practice behaviors related to successful achievement of AWCP standards.

**Technical Approach:** Soldiers enrolled in the Active Duty Weight Control Program, Fort Lewis, WA, will complete an initial and 6 month follow-up questionnaire. Questionnaires will be anonymous and information will be reported in aggregate form only with no participant identifiers.

**Progress:** All work on this project at MAMC has been completed. A final abstract from study staff at Tripler Army Medical Center is pending.



## **Detail Summary Sheets**

### **Maternal-Fetal Medicine, Department of Obstetrics/Gynecology**

### Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 202/026 **Status:** Ongoing

**Title:** Impact of Preprocedure Hydration and AFI on Success Rates of External Cephalic Version

**Principal Investigator:** CPT Robert L. Behrman, MC

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** COL Byron C. Calhoun, MC, USAF; CPT Miguel A. Brizuela, MC; LTC Peter G. Napolitano, MC

**Keywords:** Breech presentation, External cephalic version (ECV), Amniotic fluid index (AFI), Hydration

**Start Date:**

1/22/2002

**Est. Completion Date:**

Aug 03

**Periodic Review:**

**Study Objective:** (1) To elaborate upon the research performed by Dr. Kilpatrick demonstrating a link between increased maternal oral hydration and increased amniotic fluid, (2) to evaluate the effects of maternal hydration/increased AFI on the success rate of external cephalic version and (3) to contribute to the research perform by Dr Newman demonstrating factors associated with successful external cephalic version.

**Technical Approach:** Prospective, randomized blinded trial of women with singleton >37 weeks gestation in non-cephalic breech presentation. The study group will be asked to consume 2 liters of water over approximately 2 hours between 2-5 hours 2 hours prior to the anticipated version attempt. The subjects will be asked to arrive early enough in the morning for them to be observed in their consumption of fluids. The subjects in the control group will be asked to consume only 100ml of water in the same time frame and complete consumption under observation two hours prior to the procedure. If the control patient will not be able to undergo the planned procedure within two hours of the time the procedure was scheduled, the patient will be reassessed for hydration status and consideration for intravenous hydration made. The use of intravenous hydration/amounts utilized prior to version attempt will be noted in the patient's study record. Every attempt will be made to perform these procedures early in the morning to prevent a long period of NPO for the pregnant patients. The amount of fluids will not add significantly to patient discomfort and all patients will be allowed to empty their bladders as needed prior to the procedure. All subjects will be asked not to reveal to the physician attempting the version to which group they have been designated. Upon admission to labor and delivery for version attempt, urine dip will be performed to evaluate for urine specific gravity. The remainder of the procedure is standard for external cephalic version attempt. External fetal monitor will be applied and reactivity determined. Ultrasound examination will then be performed to evaluate for: non-cephalic breech presentation, position of fetal back, amniotic fluid index, and placental location. IV access will be a standard procedure and the use of a tocolytic agent will be left to the discretion of the operator and recorded. The ability to proceed to immediate Cesarean section based on maternal or fetal compromise will be available at all times. Once a reactive NST is obtained, external cephalic version attempt, either by a "forward roll" or a "backward roll" technique will be made. Version will be discontinued for excessive maternal discomfort, persistently abnormal intra-procedure fetal heart rate, and multiple unsuccessful attempts. At no time will > 4 attempts be made to perform external cephalic version. Post version NST will be obtained and documented. Plan for follow-up will include presentation at time of delivery and route of delivery for both groups. Patients who fail external version may be allowed to return for another attempt at version and be re-entered into the study. Those who receive hydration with 2 liters of fluid and those who receive only 100 mls of fluid will remain in their respective groups and not be re-randomized.

**Progress:** This protocol has not yet been initiated at MAMC. CPT Behrman assumed the role of PI for this study following the PCS of the original PI, CPT Brizuela, June 2002.



### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/094                 | <b>Status:</b> Completed             |
| <b>Title:</b> Hispanic Ethnicity and the Relationship of Ultrasound Criteria for Attributable Risk for Aneuploidy  |  |                                      |
| <b>Principal Investigator:</b> COL Byron C. Calhoun, MC, USAF  |  |                                      |
| <b>Department:</b> OB  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> CPT Jennifer A. Brown, MC; MAJ Elizabeth C. Golladay, MC; CPT Lisa M. Foglia, MC |  |                                      |
| <b>Keywords:</b> Hispanic, ethnicity, aneuploidy, ultrasound   |  |                                      |
| <b>Start Date:</b><br>6/27/2000  | <b>Est. Completion Date:</b><br>Mar 01 | <b>Periodic Review:</b><br>4/29/2002 |

**Study Objective:** To determine ultrasound growth curves from the database presently in place from the MAMC IRB approved protocol #96164 (Natural History of Gallbladder Disease in Pregnancy) and develop ethnic specific growth curves with attributable risk for aneuploidy based ultrasound derived criteria.

**Technical Approach:** This retrospective study of previously existing files will look at fetal measurements at varying times during gestation. Measurements obtained on Hispanic patients will be compared to those of Asian, Caucasian, and Black patients to determine what is considered normal growth for Hispanic patients. Predictions of aneuploidy will be evaluated against birth records as well as prenatal chromosomal analysis by amniocentesis when available. This information will allow comment on the accuracy and applicability of femur length as a minor ultrasound risk adjustment for aneuploidy specific to a Hispanic population.

**Progress:** This study was reported as completed, Apr 02. The study subgroups consisted of 63 Asian mothers, 142 black mothers, 60 Hispanic mothers, and 718 white mothers. The mean values of the variance from the expected femur length by biparietal diameter +/- 1 standard deviation were: for Asian mothers: -1.720 +/- 2.03; for the fetuses of black mothers: -0.468 +/- 1.98; for fetuses of Hispanic mothers: -0.59 +/- 6.819; and for fetuses of white mothers: -0.899 +/- 2.80. The femurs of the fetuses of the Asian, Hispanic, and black mothers were compared to white mothers: Asian versus white, P=0.0398, for the Hispanic versus white mothers, P=0.0398, and for the black versus white mothers, P=0.1221. **Conclusions:** There is a significant difference in the mean expected femur lengths by biparietal diameter among fetuses in the second trimester with regard to maternal ethnicity. Shorter femurs were noted among the fetuses of Asian and Hispanic mothers compared to the fetuses of white and black mothers. This study demonstrates further data is required for the genetic sonogram for femur length as a screening ultrasound tool.

### Detail Summary Sheet

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|------------------------|-----------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/103 | <b>Status:</b> Terminated |
|------------------------|-----------------------|---------------------------|

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**Title:** Prevalence of Anal Incontinence in New Mothers Trial (PAINT)

**Principal Investigator:** COL Gary D. Davis, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Patrick J. Woodman, MC; COL Romeo P. Perez, MC; LTC Ronald J. Place, MC; CPT Vanessa D. Dance, MC; COL Romeo P. Perez, MC

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**Keywords:** transanal ultrasound, endoanal ultrasound, endoluminal ultrasound, pregnancy, fecal incontinence, anal sphincter, sphincter disruption

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**Start Date:**

9/28/1999

**Est. Completion Date:**

Aug 00

**Periodic Review:**

3/27/2001

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**Study Objective:** To discover ways to prevent recognized and occult anal sphincter rupture and improve long-term primary closure outcome; thereby helping to prevent the development of future fecal and flatus incontinence.

**Technical Approach:** This study will investigate the occult anal sphincter disruption rate as a result of a variety of delivery types in primigravid women. The predominant method of episiotomy at MAMC is midline, which may affect the occult anal sphincter disruption rate. Primigravid women will be recruited from the OB/GYN clinic population and asked to participate postpartum. They will fill out a questionnaire, which will ask about their deliveries, their medical, surgical, colorectal histories and some randomization information. The investigator, who is blinded to the type of delivery, whether the patient had an episiotomy or tear, and other pertinent history, will perform an endoanal ultrasound of the anal musculature at approximately 6 weeks postpartum. Thickness and morphology of the internal and external sphincter and perineal body will be performed and recorded on a data sheet (attached). Those patients in which defects are found will be asked to return at approximately 6 months for repeat examination. At a later date, a second investigator will compare and verify the information requested in the patient questionnaire and obtain information about diagnoses, malposition, degree of episiotomy and extension, and labor augmentation. This will be recorded on the verification sheet. The patients will be identified by coded numbers, cross-classified to FMP/SS#. All data will be entered and analyzed using SPSS, Primer of Biostats, or similar statistical package. A small group of women (approximately 10) will be recruited to participate in an investigation on how the anal sphincter musculature morphology changes during the three trimesters of pregnancy. Each woman will undergo a series of three anal ultrasonographic examinations, one per trimester. These subjects would also the patient questionnaire, and the same data points would be obtained: Thickness and morphology of the internal and external anal sphincter and the perineal body. At the end of the trial, each woman will be asked if she would like to continue with the main study protocol, which would require a separate consent form.

**Progress:** This study was terminated by the principal investigator, 21 Aug 02, due to lack of interest after departure of the protocol's original PI.

### Detail Summary Sheet

|   |  |                           |
|---|--|---------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/095                 | <b>Status:</b> Terminated |
| <b>Title:</b> Voiding Patterns in Asymptomatic Military Women   |  |                           |
| <b>Principal Investigator:</b> COL Gary D. Davis, MC  |  |                           |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                           |
| <b>Associate Investigator(s):</b> MAJ Patrick J. Woodman, MC; Mary P. Fitzgerald, MD  |  |                           |
| <b>Keywords:</b> Urinary frequency, voiding diary, healthy females, frequency/volume chart, asymptomatic, military specific |  |                           |
| <b>Start Date:</b><br>5/22/2001   | <b>Est. Completion Date:</b><br>Feb 02 | <b>Periodic Review:</b>   |

**Study Objective:** For a racially diverse sample of American military women without lower urinary tract symptoms, our study aims to determine normal ranges for the following micturition parameters: (1) Daytime voids, (2) Nighttime voids, (3) Fluid intake (cc), (4) Largest voided volume (cc), (5) Mean voided volume (cc), (6) Daytime hourly diuresis (cc/hour), (7) Nighttime hourly diuresis (cc/hour), and (8) Voids per liter fluid intake.

**Technical Approach:** At informational lectures on “female urinary health” given during periodic female utilization training sessions, we will ask 200 female active duty soldiers to volunteer to participate in a study to determine voiding patterns in asymptomatic military women. Active duty female soldiers, ages 18-65, will be asked to volunteer for the study if they consider themselves to have “normal lower urinary tract function” (i.e. they believe they neither retain or leak urine, are not troubled by the number of times they void daily, nor by the degree of urinary urgency they experience before voiding). Volunteers will be asked to complete a questionnaire about their bladder symptoms and relevant medical history. We will also record information about subjects' age, race, MOS (job description), parity, and hormonal status. We will ask that subjects record the time and amount of any fluids they drink for 24-hours. We will also give subjects a “top-hat” to place in their toilets and ask them to record the volume of urine they pass when they visit the bathroom. We will ask subjects that they do not alter their usual intake and voiding routine during the 24-hour study period. We will then ask subjects to put the “diary” into a supplied envelope and place it in the mail. The voiding diaries will be analyzed to determine subjects' total fluid intake, number of daytime and nighttime voids, largest voided volume, mean voided volume, diuresis per hour and voids per liter fluid intake. Demographic data will also be recorded, described and compared to subjects who did not return the voiding diary.

**Progress:** This study was terminated due to the PCS of all study investigators.

### Detail Summary Sheet

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|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/046 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** Outcome of Infants Born at 22-28 Weeks Gestation: A Retrospective Review in Military Care Facilities

**Principal Investigator:** CPT Lisa M. Foglia, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** LTC Peter E. Nielsen, MC; LTC Andrew Satin, MC; LTC Michael Gordon, MC; MAJ Brian T. Pierce, MC

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**Keywords:** Neonatal morbidity, Neonatal mortality, Preterm delivery, Gestational age, Respiratory Distress Syndrome, Necrotizing Enterocolitis, Sepsis, Intraventricular hemorrhage

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**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
1/31/2002

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**Study Objective:** To analyze and report neonatal morbidity and mortality in early gestation in military care facilities.

**Technical Approach:** All neonates born between 22 and 28 weeks EGA, inclusive, will be identified through hospital coding systems. A chart review will be performed on both the mother and neonate. Data will be collected to include: Gestational age at delivery, delivery weight antepartum betamethasone administration, neonatal surfactant administration, maternal age and race, and specific neonatal complications to include: death, RDS, WH (grade 3 and 4), periventricular leukomalacia, NEC, hyperbilirubinemia requiring phototherapy or exchange transfusion, retinopathy of prematurity, hypoglycemia, and sepsis. Maternal medical problems and ante/intrapartum complications will also be recorded. A follow-up study is planned to report long term follow up in these premature infants, specifically at 2 years of age and 5 years of age. The data will be collected on a separate data sheet (attached), with the patient being identified by a code number. The principle investigator will be the sole keeper of the names of the patients as well as the code to which they are assigned.

**Progress:** 62 charts were reviewed during FY02. An abstract presentation of the results from these 62 patients has been submitted to the 2002 ACOG Armed Forces District Meeting scheduled for Oct 02.

### Detail Summary Sheet

|  |  |                                      |
|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/106                 | <b>Status:</b> Terminated            |
| <b>Title:</b> Tubal sterilization with the Ligasure Vessel Sealing System  |  |                                      |
| <b>Principal Investigator:</b> CPT Lisa M. Foglia, MC  |  |                                      |
| <b>Department:</b> OB  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> CPT Louis A. Dainty, MC; LTC Peter E. Nielsen, MC; COL Milo L. Hibbert, MC; CPT Ruth A Reardon, MC |  |                                      |
| <b>Keywords:</b> LigaSure Vessel Sealing System, fallopian tubes, bilateral tubal occlusion  |  |                                      |
| <b>Start Date:</b><br>6/27/2000  | <b>Est. Completion Date:</b><br>Jul 01 | <b>Periodic Review:</b><br>5/20/2002 |

**Study Objective:** To determine whether the Ligasure Vessel Sealing System may be used to effectively seal fallopian tubes as evidenced by gross and histological examination.

**Technical Approach:** Subjects will have a preoperative evaluation that will include obtaining a history, physical examination, preoperative anesthesia visit, and laboratory studies (CBC, hCG). Subjects will be randomized on a 1:1:1 basis to three different treatment groups - 1 seal per Fallopian tube, 2 seals per Fallopian tube, 3 seals per Fallopian tube with the Ligasure device. A laparoscopic tubal ligation will be performed. A mid-isthmus segment of the right Fallopian tube will be identified. The Ligasure device will be inserted through the suprapubic port, and a mid-isthmus segment of Fallopian tube will be grasped with the Ligasure device. It will be sealed one, two or three times depending upon which group the patient was assigned to. The Ligasure device will be removed and then a laparoscopic Pomeroy will be performed where the ligated segment of tube is excised and removed. The length of the tubal segment removed will not be altered by the Ligasure procedure.

The segments of Fallopian tube will be submitted to Pathology, as per usual for the Pomeroy procedure. The tubal diameter (lumen and external diameter), length of tubal occlusion, and length of tissue damage beyond the length of tubal occlusion will be measured in millimeters. The tubal segments will be examined histologically for extent of spread of tissue damage. Presence or absence of tubal occlusion will be determined by ability to cannulate the tubes with a lacrimal duct probe and then by histologic examination of the tube. The presence/absence of tubal occlusion will be compared by group. The length of tubal occlusion and length of tissue damage beyond the length of tubal occlusion will be compared by group, using the ANOVA.

**Progress:** Due to lack of funding, the principal investigator terminated this study at MAMC prior to its initiation.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 99/077      **Status:** Ongoing

**Title:** Misoprostol for the Medical Management of Non-viable First Trimester Pregnancies

**Principal Investigator:** CPT Robert G. Fowers, MC

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** MAJ Jason D. Parker, MC; COL Milo L. Hibbert, MC; LTC Peter E. Nielsen, MC; Troy H. Patience, B.S.; CPT Louis A. Dainty, MC

**Keywords:** Spontaneous abortions, non-viable pregnancy, misoprostol

**Start Date:**

6/22/1999

**Est. Completion Date:**

Mar 01

**Periodic Review:**

9/24/2002

**Study Objective:** The purpose of this study is to examine the effectiveness of misoprostol (Cytotec; GD Searle and Co., Chicago, IL) for the management of non-viable first trimester pregnancies. Specifically, misoprostol (15-S-15-methyl PGE1) will be compared to a placebo with expectant management in who have documented non-viable gestations. We will examine the following outcome variables: time to resolution, number of patients requiring dilation & curettage, change in hematocrit, cost to the institution, patient satisfaction, and reported side effects.

**Technical Approach:** Patients presenting to the OB/GYN clinic with a nonviable gestation will be considered potentially eligible to participate in the study. Those patients entering the study will be directed to the OB/GYN clinic for evaluation, exam, counseling and to watch the video giving explanation of purpose of the study and the planned procedure, but also expected side effects and possible complications. An anembryonic gestation will be diagnosed in any patient with an irregularly shaped gestational sac and mean sac diameter of 16 or greater without an embryonic pole. Additionally any patient with an intrauterine fetal pole between 5 and 14 mm with no cardiac activity will be considered non-viable and will be considered for acceptance into our study. After explanation of the study, patients will view a short video to ensure consistency of counseling. Upon conclusion of the counseling and video, patients will be asked to sign a consent form for participation in the study. Complete history and physical will be performed and initial laboratory will be obtained to include CBC, BUN, creatinine, quantitative BHCG and blood type to include Rh status. Patients will then be randomized into two groups: study group receiving misoprostol per vagina and the control group receiving a placebo per vagina. Subjects will be issued an envelope and asked to report to the pharmacy where they will pick up their study medication, which will be blinded to them and the provider. Additionally, they will be given Motrin and Phenergan to help alleviate undesired side effects. Subjects will have four 200 ug tablets of misoprostol in the posterior fornix of the vagina using a speculum under the direct visualization of the provider. Patients will be asked to return in 24 hours for re-examination to include a pelvic ultrasound using a vaginal probe. If no evidence of an intrauterine pregnancy remains (i.e. gestational sac, fetal pole etc.), patients will be informed that their miscarriage was complete, given precautions and asked to make an appointment for follow-up in 4 weeks in addition to weekly visits to the lab for quantitative BHCG. All patients will be followed until the quantitative BHCG has fallen zero to ensure resolution of the pregnancy event. Those patients with evidence of a gestational sac will be given a second dose of misoprostol or alternatively a D&C if they choose to withdraw from the study or surgical intervention is deemed clinically indicated by the attending staff. Again, the subjects will be given appropriate counseling and precautions and asked to follow up in an additional 24 hours for re-evaluation. Surveys will be given at each visit and follow up to evaluate patient satisfaction and also to query for unintended side effects and complications.

**Progress:** Four patients enrolled during FY02 for a total enrollment of 14 since study approval. No adverse outcomes or reactions occurring to date. Enrollment continues.

### Detail Summary Sheet

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|--|--|--------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/055                 | <b>Status:</b> Completed |
| <b>Title:</b> Assessing the Interrater Reliability of the Military Tape Test for Body Fat Composition Compared to the Near-Infrared Interactance for Accuracy of Body Fat Measurement  |  |                          |
| <b>Principal Investigator:</b> CPT Jennifer L. Gotkin, MC  |  |                          |
| <b>Department:</b> OB  | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> LTC Peter E. Nielsen, MC   |  |                          |
| <b>Keywords:</b> body fat comparison military tape test anthropometrics, military specific   |  |                          |
| <b>Start Date:</b><br>3/26/2002  | <b>Est. Completion Date:</b><br>Apr 02 | <b>Periodic Review:</b>  |
| <b>Study Objective:</b> Determine the interrater reliability and validity of the tape test compared to the near-infrared interactance (NIR) for measurement of bodyfat composition.  |  |                          |
| <b>Technical Approach:</b> Subjects volunteering for body fat composition at the 4.3 mile race will be asked to participate in body fat composition study and will be subjected to an additional two body fat measurements using the Army standard tape test in addition to the light density test performed by the nutrition clinic personnel. The subjects who participate will fill out a demographics sheet and will receive a number and 3 measurement sheets. After each measurement the sheet will be collected by an independent party and the subject will continue with the measurements until two tap measures and one light density measurement have been completed. |  |                          |
| <b>Progress:</b> A total of 25 subjects enrolled in this study at MAMC. Study is now completed. An abstract is pending.  |  |                          |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 99/035      **Status:** Ongoing

**Title:** Comparison of Elective Labor Induction and Spontaneous Labor: A Randomized, Controlled Clinical Trial

**Principal Investigator:** MAJ Bobby C. Howard, MC, USAF

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** CPT Robert H. G. Holland, MC; COL Paul N. Smith, MC; MAJ Brian T. Pierce, MC; MAJ Richard Wagner, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF; COL Romeo P. Perez, MC; Kathleen M. Judge, RN; Roxanne Piecek, RN; CPT Miguel A. Brizuela, MC; MAJ Christina C Apodaca, MC; CPT Penny L. Larson, MC

**Keywords:** Elective induction, spontaneous labor, maternal outcomes, neonatal outcomes

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
9/24/2002

**Study Objective:** The purpose of this study is to compare cesarean section rates between patients delivered at term with a favorable cervix by elective induction with patients allowed to enter labor spontaneously. Additional maternal and neonatal outcomes will also be compared between the two groups.

**Technical Approach:** Between 38 and 39 weeks, subjects presenting with a favorable cervix and consenting to be in the study, will be randomized into either the labor induction group or the spontaneous labor group. Labor induction will follow MAMC Labor and Delivery protocol. Those subjects assigned to labor induction will be scheduled within 72 hours for admission including routine admission labs, establishment of intravenous access and fetal monitoring. Subjects in the control group will continue in the Obstetric Clinic until the onset of spontaneous labor. Their labor will also follow MAMC Labor and Delivery protocol. Subject information sheets for the health care providers managing the subjects will capture complete documentation of labor and delivery information. These data will be entered into a computer database for analysis and the data sheets will not be part of the subject's medical record. Subjects will also be asked to fill out a questionnaire, the Labor and Delivery Satisfaction Index, to assess satisfaction with their labor and delivery. Chi-square analysis will be used to assess for differences in nominal variables (epidural use, oxytocin use, chorioamnionitis, postpartum complications, NICU admissions, meconium stained amniotic fluid, neonatal or maternal complications, neonatal or maternal birth trauma). The paired Student's t-test will be used to compare groups of continuous variables (cesarean section rate, vaginal delivery rate, operative vaginal delivery rate, duration of first and second stage of labor, maternal and neonatal lengths of stay, birth weight, Apgar scores).

**Progress:** A total of 226 patients have been enrolled to date. The study is approaching an interim analysis and anticipate some preliminary data within the next 3-4 months based on enrollment.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/022                 | <b>Status:</b> Completed |
| <b>Title:</b> The Effects of a Cyclooxygenase II Inhibitor on Prostacyclin and Thromboxane A2 Production by Placental Arteries From Normal and Preeclamptic Patients |  |                          |
| <b>Principal Investigator:</b> MAJ Bobby C. Howard, MC, USAF   |  |                          |
| <b>Department:</b> OB  |  | <b>Facility:</b> MAMC    |
| <b>Associate Investigator(s):</b> COL Byron C. Calhoun, MC, USAF; LTC Peter G. Napolitano, MC  |  |                          |
| <b>Keywords:</b> angiotensin II, peroxides, cyclooxygenase II inhibitor, preeclampsia, placenta  |  |                          |
| <b>Start Date:</b><br>1/22/2002  | <b>Est. Completion Date:</b><br>Jan 02 | <b>Periodic Review:</b>  |

**Study Objective:** To determine the effects of a cyclooxygenase II inhibitor on placental artery production of prostacyclin and thromboxane A2 from normal and preeclamptic patients following exposure of the arteries to angiotensin II or t-butyl hydroperoxide.

**Technical Approach:** This study will evaluate the ratio of TxA2 to PGI2 production by placental arteries from normal pregnancies and preeclamptic pregnancies following exposure of the vessels to peroxide and angiotensin II in tissue culture. Additionally, the vessels will be treated with rofecoxib, a selective COX II inhibitor, and evaluate the TxA2 and PGI2 levels following exposure of the vessels to peroxide and angiotensin II.

**Progress:** Data collection and evaluation have been completed. The study identified cyclooxygenase II inhibition adversely affects the thromboxane to prostacyclin ration and decreases production of prostacyclin. Abstract is available.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/030 | <b>Status:</b> Ongoing |
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**Title:** Effect of Angiotensin II on Fetal Placental Perfusion Pressures in Preeclampsia Ex Vivo Cotyledon

**Principal Investigator:** MAJ Christine M. Kovac, MC

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Brian T. Pierce, MC; MAJ Elizabeth C. Golladay, MC; LTC Peter G. Napolitano, MC; COL Byron C. Calhoun, MC, USAF; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC

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**Keywords:** Preeclampsia, Angiotensin II, dual perfusion placental cotyledon model

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**Start Date:**  
1/23/2001

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
12/2/2002

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**Study Objective:** To use the dual perfused placental cotyledon model to investigate perfusion pressure changes induced by angiotensin II in fetoplacental vasculature of preeclamptic placentas pretreated with low dose acetylsalicylic acid, compared to controls.

**Technical Approach:** We will obtain 10 placentas from patients who meet strict criteria for preeclampsia, and 10 patients without preeclampsia who otherwise meet our inclusion and exclusion criteria. We will perfuse a cotyledon in our placental perfusion lab and measure the baseline perfusion pressure as well as the response of the cotyledon to a low and high dose of angiotensin II with and without treatment of low dose acetylsalicylic acid.

**Progress:** Since the last review in October, an additional control has been run, requiring another control and another preeclamptic placenta to complete data. Addendum to analyze IL-18 assays on the effluents is still being written, to run when all samples are complete. Initial data has been presented at the AFD district meeting of ACOG. Anticipate presenting final data at the annual SMFM meeting in February.

### Detail Summary Sheet

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|---|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/065                 | <b>Status:</b> Ongoing              |
| <b>Title:</b> Effect of Low-Dose Acetylsalicylic Acid and Angiotensin II on Fetal Placental Perfusion Pressures in the Preeclamptic Ex Vivo Cotyledon   |  |                                     |
| <b>Principal Investigator:</b> MAJ Christine M. Kovac, MC   |  |                                     |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                     |
| <b>Associate Investigator(s):</b> MAJ Brian T. Pierce, MC; MAJ Elizabeth C. Golladay, MC; LTC Peter G. Napolitano, MC; COL Byron C. Calhoun, MC, USAF; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC   |  |                                     |
| <b>Keywords:</b> preeclampsia, placental perfusion pressure, angiotensin, low-dose aspirin  |  |                                     |
| <b>Start Date:</b><br>2/27/2001   | <b>Est. Completion Date:</b><br>Jul 01 | <b>Periodic Review:</b><br>1/8/2002 |
| <b>Study Objective:</b> To use the dual perfused placental cotyledon model to investigate perfusion pressure changes induced by angiotensin II in fetoplacental vasculature of preeclamptic placentas pretreated with low dose acetylsalicylic acid, compared to controls.  |  |                                     |
| <b>Technical Approach:</b> This study will obtain 10 placentas from patients who meet strict criteria for preeclampsia, and 10 patients without preeclampsia who otherwise meet our inclusion and exclusion criteria. Investigators will perfuse a cotyledon in the MAMC placental perfusion lab and measure the baseline perfusion pressure as well as the response of the cotyledon to a low and high dose of angiotensin II with and without treatment of low dose acetylsalicylic acid. |  |                                     |
| <b>Progress:</b> Five placentas were used during FY02 for a total of 7 on this study. Control placentas run with other protocol. Will need to run aspirin with preeclamptic placentas.  |  |                                     |

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/096 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

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**Title:** The Effects of Hypoxia and Hypoxia With Acidemia on Placental Production of Adrenomedullin in the Isolated Dually Perfused Placental Cotyledon

**Principal Investigator:** MAJ Christine M. Kovac, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Brian T. Pierce, MC; MAJ Christina C Apodaca, MC; LTC Peter G. Napolitano, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF

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**Keywords:** adrenomedullin, placenta, hypoxia, acedemia

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**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
5/20/2002

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**Study Objective:** To determine if adrenomedullin levels are increased in placental cotyledons exposed to hypoxic and academic conditions.

**Technical Approach:** Cotyledons from a total of 20 placentas will be obtained from patients with uncomplicated term vaginal and caesarian deliveries. Maternal and fetal circulations of the cotyledons will be perfused with a solution of Hank's Balanced Salt Solution, bovine albumin, heparin and gentamicin. The 2 cotyledons from the first 10 placentas will be perfused, one with hypoxic solution and the other (control) with physiologic solution. Two cotyledons each from the next 10 placentas will be perfused, one with hypoxic and academic solution and the other (control) with physiologic solution. After perfusion of an intact fetoplacental circuit has been established, effluents will be collected at hourly intervals for four hours. These samples will be batched and stored for adrenomedullin quantitation, using an ELISA. Fetoplacental vascular tone will be continuously monitored throughout the experiment and will be recorded at ten-minute intervals. Data will be analyzed using repeated measure analysis of variance.

**Progress:** All work on this bench study has been completed and data presented at SMFM 2002, pending publication.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 99/051

**Status:** Terminated

**Title:** The Use of Transvaginal Sonography in Predicting Preterm Delivery in Patients with Preterm Contractions

**Principal Investigator:** MAJ Christine M. Kovac, MC

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** CPT Lisa M. Foglia, MC; MAJ Brian T. Pierce, MC; MAJ Richard Wagner, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF; Troy H. Patience, B.S.; MAJ Christina C Apodaca, MC

**Keywords:** Preterm labor, transvaginal sonography, digital cervical exam

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Aug 99

**Periodic Review:**  
5/20/2002

**Study Objective:** Primary: To investigate the accuracy of transvaginal cervical ultrasound in predicting the occurrence of preterm delivery, in patients presenting to Labor and Delivery with complaints consistent with preteen contractions. Secondary: We will also compare the abilities of transvaginal sonography and digital cervical exam in predicting preterm delivery within one week from examination.

**Technical Approach:** Despite recent advances in modern obstetric care, the incidence of preterm delivery has not decreased, and remains a leading cause of neonatal morbidity and mortality. Due to the refractory nature of preterm labor to effective management, early diagnosis is essential. Definitive diagnosis of legitimate preterm labor remains difficult, however, and results in over-diagnosis and treatment of what is most likely innocuous preterm contractions. Early cervical effacement and dilation may be subtle changes that may not be identified on digital examination. Transvaginal cervical ultrasonography is a precise, reproducible, modality that can provide an objective means by which to evaluate the cervix for early effacement and dilation. While studies have identified the utility of transvaginal cervical sonography in predicting preterm delivery, its role in assessing patients with preterm contractions is less clear. We propose to evaluate the utility of transvaginal cervical sonography in predicting subsequent preterm labor and delivery. We will also compare the efficacy of cervical sonography with digital examination in predicting the incidence of preterm delivery. We hope to identify a cervix length in a patient with preterm contractions, at which a physician can feel comfortable sending her home, with a 98 to 100 percent assurance that she will not deliver within the next week (eg, that cervix length which yields a 98 to 100 percent negative predictive value for preterm delivery within a week).

**Progress:** Protocol has been terminated due to difficulty in recruiting sufficient patients for number of participants needed.

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/055 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** Fetal Growth Curves in a Military Population

**Principal Investigator:** LTC Peter G. Napolitano, MC

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** MAJ Brian T. Pierce, MC; MAJ Richard Wagner, MC; MAJ Elizabeth C. Golladay, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF; MAJ Christina C Apodaca, MC; CPT Dawn E. Elliot, MC

**Keywords:** fetus, growth, ultrasound, fetal weight, birthweight, military specific

**Start Date:**

3/28/2000

**Est. Completion Date:**

Dec 00

**Periodic Review:**

1/31/2002

**Study Objective:** To determine the range of in utero fetal weight throughout pregnancy using actual data, including birth weights, for a cohort at sea level using a database presently in place from the MAMC IRB approved protocol #96164 (natural history of gallbladder disease in pregnancy) and develop specific growth curves relevant to our population.

**Technical Approach:** Retrospective review of previously existing files and medical records. Data collected will include sonographic measurements of active duty women and military health care beneficiaries, plus maternal age, ethnic origin, smoking status, monthly income, neonatal gender and neonatal birth weight.

**Progress:** Work on this protocol has been completed. Data from 100 ultrasound examinations during labor were collected as per a protocol revision. The data has been analysed and paper written and the study will be presented this month at the Armed Forces District Meeting of the American College of Obstetrics and Gynecology, in Honolulu Hawaii by Dr Dawn Elliot. The paper is planned to be submitted for publication. An abstract is available.

### Detail Summary Sheet

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|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/015                 | <b>Status:</b> Completed              |
| <b>Title:</b> Myometrial Gap Junctions and Their Importance in Obstetric Patients with Chorioamnionitis   |  |                                       |
| <b>Principal Investigator:</b> LTC Peter G. Napolitano, MC  |  |                                       |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> COL Byron C. Calhoun, MC, USAF; MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; Alan F. Lau, Ph.D.; MAJ Christina C Apodaca, MC; MAJ Richard Wagner, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC |  |                                       |
| <b>Keywords:</b> Chorioamnionitis, myometrial gap, Cx43 protein, Cx 43mRNA, amniorrhexus  |  |                                       |
| <b>Start Date:</b><br>11/19/1999  | <b>Est. Completion Date:</b><br>Oct 00 | <b>Periodic Review:</b><br>10/23/2001 |

**Study Objective:** The purpose of this study is to investigate whether decreased connexin 43 mRNA and/or protein levels and the decreased formation of gap junction plaques in the myometrium is responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

**Technical Approach:** Myometrial tissue will be obtained during cesarean section from laboring patients with and without chorioamnionitis, and from those patients requiring cesarean section prior to the onset of labor (without chorioamnionitis). Cx43 messenger RNA and protein levels will be compared among these patients and immunohistochemistry will be performed to examine the presence of gap junction plaques. Decreased Cx43 mRNA and protein levels and decreased gap junction formation in the myometrium of chorioamnionitis patients may lead to decreased gap junctional communication (GJC) in the myometrium. This decreased GJC may be responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

**Progress:** No additional enrollment occurred during FY02 and the protocol has been reported as completed. Dr Pierce is presenting this study this month at the Armed Forces District meeting of the American College of Obstetrics and Gynecology annual meeting. An abstract from the meeting will be submitted to DCI.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/023 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** Delayed Maternal Pushing with Labor Epidural Analgesia: Effects on Operative Vaginal Delivery

**Principal Investigator:** LTC Peter E. Nielsen, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** CPT Richard O. Burney, MC; MAJ Brian T. Pierce, MC; MAJ Christina C Apodaca, MC; MAJ Richard Wagner, MC; LTC (Ret.) Sylvia Wood, RN; Thomas W. Overly, RN, CRNA; COL Byron C. Calhoun, MC, USAF; Kathleen M. Judge, RN; CPT Robert W. Chalmers, MC

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**Keywords:** Vaginal delivery, maternal pushing, epidural analgesia

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|--------------------|------------------------------|-------------------------|
| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
|--------------------|------------------------------|-------------------------|

1/26/1999

Feb 00

11/12/2002

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**Study Objective:** To determine the effect of delayed maternal pushing on the rate of operative vaginal delivery.

**Technical Approach:** Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects will be randomized into one of two treatment groups after the placement of epidural analgesia; early pushing and delayed pushing. Early pushing group: Subjects will be allowed to push at the first maternal urge once the cervix is completely dilated. Delayed pushing group: Subjects will begin pushing when the vertex is distending the perineum. The subjects in this group will be given 0.25% bupivacaine epidural boluses to delay the maternal urge to push. Cervical examinations in both groups will occur at either maternal urge to push, or at 2 hours following complete cervical dilation. If no maternal urge to push at 2 hours, and the descent of the vertex is  $\geq 1$  cm/hr, then continue management as randomized. If descent  $< 1$  cm/hr, then begin oxytocin infusion per protocol for hypo tonic contractions and reexamine cervix in 2 hours, or at the onset of urge to push. If uterine activity is adequate, then begin pushing in both groups. Reexamine cervix in 2 hours and evaluate for arrest of descent. This management may allow the length of the second stage to be extended to approximately 5 hours, exceeding the generally accepted length of 3 hours in nulliparas and 3 hours in multiparas with epidural analgesia. The type of operative intervention (forceps, vacuum or cesarean delivery) will be the decision of the attending physician to ensure a safe and effective delivery.

**Progress:** Three subjects enrolled during FY02 for a total enrollment of 59 overall. Enrollment remains ongoing. Investigators are considering the addition of another study site to help with accrual.



### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 99/024                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> Extending the Duration of Active Phase Arrest: Effects on Cesarean Delivery   |  |                                      |
| <b>Principal Investigator:</b> LTC Peter E. Nielsen, MC   |  |                                      |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> CPT Amy J. Asato, MC; MAJ Brian T. Pierce, MC; MAJ Christina C Apodaca, MC; MAJ Richard Wagner, MC; Thomas W. Overly, RN, CRNA; COL Byron C. Calhoun, MC, USAF  |  |                                      |
| <b>Keywords:</b> labor, active phase arrest, cesarean delivery  |  |                                      |
| <b>Start Date:</b><br>1/26/1999   | <b>Est. Completion Date:</b><br>Feb 00 | <b>Periodic Review:</b><br>2/26/2002 |
| <b>Study Objective:</b> To determine the effect of extending the length of active phase arrest of dilation from 2 to 4 hours on the rate of cesarean delivery.  |  |                                      |
| <b>Technical Approach:</b> Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects with active phase arrest, despite 2 hours of adequate uterine activity and continuous labor epidural analgesia, will be randomized to either cesarean delivery or 2 additional hours of labor. All subjects at the end of this 2 hour study period who fail to demonstrate cervical change (< 1 cm progress in 2 hours) will be delivered by cesarean section. All other patients will continue the labor process. Cesarean delivery for non reassuring fetal heart rate tracing will be performed based on routine obstetric indications. |  |                                      |
| <b>Progress:</b> Five subjects enrolled during FY02 for a total enrollment of 17 subjects overall, with no adverse events reported. Enrollment remains ongoing.   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/031 | <b>Status:</b> Ongoing |
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**Title:** Relationship of Cesarean Delivery for Arrest of Descent and Station at Onset of Maternal Pushing: A Case Control Study

**Principal Investigator:** LTC Peter E. Nielsen, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** CPT Craig Frayer, MC; LTC (Ret.) Sylvia Wood, RN; COL Roderick F. Hume, MC; CPT Richard O. Burney, MC

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**Keywords:** Cesarean delivery, arrest, maternal pushing

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**Start Date:**

2/23/1999

**Est. Completion Date:**

Apr 99

**Periodic Review:**

9/24/2002

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**Study Objective:** To determine the effect of station at onset of second stage on the rate of cesarean delivery in primiparous patients with epidural anesthesia.

**Technical Approach:** Using the 1996/1997 labor and delivery records of deliveries at MAMC, a case control study will be performed. All primiparous patients with epidural anesthesia who required a cesarean section for arrest of descent will be identified and labeled as cases. For each case, two primiparous patients with epidural anesthesia who progressed to spontaneous delivery will be identified and labeled as controls. For each case, respective controls will be matched for maternal age, gestational age, fetal weight and use of oxytocin in labor. During this period of labor management, all patients began pushing efforts at the onset of the second stage, which was defined as cervical progression to complete effacement and complete dilation irrespective of fetal station. The fetal station at the onset of second stage will be determined for all cases and controls. A chi-square analysis will be performed to compare cases and controls with second stage maternal pushing efforts begun at fetal station 0 and higher. This will be conducted so as to allow the determination of an odds ratio for operative delivery when maternal pushing efforts are begun at fetal station higher or equal to 0. Additionally, each station will be assigned a value to allow for the performance of the Mann-Whitney Rank Sum Test in the comparison of cases and matched controls.

**Progress:** 30 records were reviewed during FY00. No additional information was collected during FY 01 or FY02. Study remains ongoing for data collection with anticipated initiation of chart reviews soon.

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 99/102

**Status:** Terminated

**Title:** Comparison of Tolterodine and Oxybutinin for the Treatment of Urinary Incontinence Among Female Soldiers

**Principal Investigator:** LCDR Amy L. O'Boyle, MC, USNR

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick J. Woodman, MC; COL Milo L. Hibbert, MC; CPT Vanessa D. Dance, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; Dennis A. Kelly, Ph.D.; LTC (Ret) Richard A. Sherman, Ph.D.; COL Gary D. Davis, MC; COL Robert E. Ricks, MC

**Keywords:** urinary incontinence, Tolterodine, Oxybutinin, soldiers, women, drug therapy, military specific

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
9/25/2001

**Study Objective:** (1) To determine the relative effectiveness of Tolterodine and Oxybutinin in the treatment of urinary urge incontinence in female soldiers during exercise, (2) to determine incidence and severity of anticholinergic side effects of Tolterodine and Oxybutinin in female soldiers, (3) to determine whether Tolterodine and Oxybutinin have significant cognitive effects on work performance tasks, and (4) to determine changes in quality of life and work performance during treatment of urinary urge incontinence with Tolterodine and Oxybutinin.

**Technical Approach:** Sixty active duty female soldiers with urge incontinence will be recruited through a letter sent to all female soldiers at Fort Lewis. Each subject will initially undergo a urodynamic evaluation, which includes uroflometry, with post-void residual urine volume measurement, retrograde provocative water cystometry, resting and stressed urethral axis determination, and direct visualization testing of fluid loss with stress. Urethral pressure profilometry with urethral closure pressures will also be performed. The subjects will then be evaluated one week later with ambulatory cystometric recordings. The subjects will be fitted with the UPS 2020 ambulatory measurement system. The intravesical and intravaginal pressures will be recorded with flexible 3mm microtip inserted 6cm from the urethral meatus and above the levator plate vaginally. The subjects will be given instructions to record events on the ambulatory urodynamic recording system as they occur, and to proceed with the work or exercise which commonly produce their urinary incontinence. All subjects will be asked to complete a standard questionnaire which will assess the number and severity of the incontinent episodes they are experiencing. In addition, they will complete a standard questionnaire which will assess job satisfaction and a standard quality of life survey. Subjects will be randomly assigned to one of 3 groups: Group I - Twenty subjects will receive placebos (one tablet twice/day), Group II - Twenty subjects will receive Oxybutinin (5mg twice/day), Group III - Twenty subjects will receive Tolterodine (1 mg twice/day). All subjects will be re-tested after one week of therapy by both stationary and ambulatory urodynamic studies. Comparison will be made among the groups as to the reduction of the amplitude and frequency of uninhibited detrusor contractions. The subjects will repeat the standard questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise. All subjects who still complain of urinary urge incontinence at the end of one week of therapy will have their medication increased as follows: Group I - Increased to two tablets twice/day, Group II - Oxybutinin increased to 5 mg three times/day, Group III - Tolterodine 2mg twice/day. All subjects will be re-tested at the end of the second week of therapy. Comparisons will be made among the groups as to the reduction of the amplitude and frequency of inhibited detrusor contractions. The subjects will repeat the standard questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise.

**Progress:** This study has been reported as terminated at MAMC, 16 Sep 02, due to the PCS of Associate Investigator, COL Gary Davis.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/016 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

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**Title:** The Degree of Pelvic Relaxation in a General Population of Female Subjects

**Principal Investigator:** LCDR Amy L. O'Boyle, MC, USNR

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Patrick J. Woodman, MC; Steven E. Swift, M.D.; Susan Jackson, M.D.; Margie A. Kahn, M.D.; Val Y. Vogt, M.D.; Michelle M. Germain, M.D.; Michael T. Valley, M.D.; Mary Milner, Project Manager; Joseph Schaffer, M.D.; Marie Fidela R. Paraiso, M.D.; Deirdre R. Bland, M.D.

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**Keywords:** prolapse, pelvic exam, military specific

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**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
10/23/2001

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**Study Objective:** To describe the degree of pelvic organ support in subjects presenting to nine geographically separate Obstetrics and Gynecology clinics requiring, as part of their visit, a routine pelvic exam to meet the requirements of annual gynecological health care and to evaluate the correlation of pelvic support to specific symptomatology associated with severe pelvic organ prolapse.

**Technical Approach:** Once subjects consent to be part of the study, during the standard pelvic exam a series of measurements to determine degree of pelvic relaxation will be performed as the subject performs a Valsalva or cough. These measurements will be recorded on a data collection sheet. Various biographical data will be collected and subjects will be asked 20 questions regarding their symptoms associated with pelvic prolapse. Data collected from this study will be used as an initial step in documenting the degree of pelvic organ support in a general population and analyze various suspected etiologic factors for the development of severe pelvic organ prolapse.

**Progress:** No patients enrolled during FY02. Data analysis is being performed on the 110 enrollees. This study is completed. An abstract will be submitted to DCI when available.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/058

**Status:** Ongoing

**Title:** The Effect of Prenatal Pelvic Floor Exercises on Postpartum Pelvic Floor Function: A Two Phase Study

**Principal Investigator:** LCDR Amy L. O'Boyle, MC, USNR

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; LTC (Ret) Richard A. Sherman, Ph.D.; CPT Vanessa D. Dance, MC; CPT Lisa M. Foglia, MC; COL Robert E. Ricks, MC

**Keywords:** pelvic floor, musculoskeletal pain, urinary incontinence, fecal incontinence, biofeedback, Kegel

**Start Date:**  
3/28/2000

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
3/26/2002

**Study Objective:** To determine whether the performance of pelvic floor strengthening and control exercises (Kegel exercises and electromyographic biofeedback from the pelvic floor) prior to giving birth for the first time (primiparous) can (1) effect pelvic floor function (as measured by POPQ and transanal sonography) and urodynamic testing (UCMG - urocystometrogram) (2) decrease the occurrence and intensity of common pelvic floor problems occurring after delivery including pelvic organ prolapse, urinary incontinence, and fecal incontinence. Within this overall objective, to determine whether addition of home-use surface electromyographic (muscle tension) biofeedback devices to standard Kegel exercises will decrease the rate and intensity of problems.

**Technical Approach:** The first phase of this study will be a ten-subject open pilot to refine techniques. Each participant will perform the exercises for at least one month prior to delivery and at least two months afterwards. Feedback about the procedures and patient attitudes will be evaluated. The second phase will recruit a total 60 first-delivery mothers to three different arms of the study. Each participant will randomly be assigned to: no prescribed pelvic floor exercises in addition to standard counseling (normal treatment control group), instructed Kegel exercises (practiced at home for at least one month prior to delivery) in addition to standard counseling, or instructed Kegel floor exercises and use of the Persist Pelvic Floor trainer (a biofeedback device) at home in addition to standard counseling.

Data from all three groups will be compared to determine the effect of supplemented instruction on postpartum pelvic floor function.

**Progress:** Ten subjects enrolled in this study at MAMC during FY01; however, there was no patient enrollment during FY02 due to time constraints of the study investigators. The principal investigator plans to add new associate investigators to help with future subject enrollment.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 201/096

**Status:** Ongoing

**Title:** The Effects of Pregnancy and Delivery on Pelvic Organ Support in Nulliparous Pregnant Females

**Principal Investigator:** LCDR Amy L. O'Boyle, MC, USNR

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** MAJ Elizabeth C. Golladay, MC; COL Byron C. Calhoun, MC, USAF; COL Gary D. Davis, MC; COL Robert E. Ricks, MC; CPT Melissa V. Terry, MC; LCDR Mary G. Battaglia, NC, USNR; MAJ Geoffrey Towers, MC

**Keywords:** pelvic floor, urinary incontinence, fecal incontinence, pelvic organ prolapse, POPQ, military specific

**Start Date:**  
5/22/2001

**Est. Completion Date:**  
Sep 03

**Periodic Review:**  
4/23/2002

**Study Objective:** The purpose of this study will be to measure the degree of pelvic organ support in nulliparous pregnant females throughout gestation and following delivery, and to assess the affect of obstetric variables on pelvic organ support.

**Technical Approach:** Consenting subjects will undergo an exam to assess stage of pelvic support as measured by the POPQ (Pelvic Organ Prolapse Quantification), and 3-D ultrasound of the pelvic floor anatomy will be performed in the first and third trimesters and post-partum visit (approximately 8 weeks). The POPQ is performed at the same time as a pelvic examination. Nine points in the vagina are measured, in centimeters, relative to the hymen, at the same time that the pelvic exam is performed. These nine points are as follows (GH, PB, Aa, Ba, Ap, Bp, C, D, TVL). GH and PB correspond to the genital hiatus and perineal body. These are measured immediately prior to the pelvic exam. Points Aa, Ba, Ap and Bp correspond to points on the anterior and posterior vaginal walls. Points C refers to the cervix, D to the posterior culdesac and TVL is the total vaginal length. Once derived, a stage is assigned 0, I, II, III or IV. Endoanal ultrasound involves inserting a small probe into the external anal canal. The presence of a break or defect of the circumferential internal and external anal sphincters is measured and quantified by degrees of separation. POPQ is routinely performed at the time of pelvic exam in the Pregnant Soldier Wellness Clinic. Endoanal ultrasound, and 3-D ultrasound are not routinely performed. Endoanal is routinely used however in evaluating patients post-partum who have had traumatic deliveries, and in all patients with symptoms of anal incontinence. At each evaluation, patients will answer questionnaires pertaining to symptoms of pelvic organ support, urinary symptoms and fecal symptoms.

**Progress:** 93 subjects enrolled in this study at MAMC. The average age of the population was 22.4 years (range 18-31 years). A total of 126 exams were performed, 59 in the first trimester, 26 in the second trimester, and 41 in the third trimester. Sixteen subjects had exams performed in both the first and third trimesters. Comparison of POPQ stage between the first and third trimesters was found to be significantly higher in the trimester compared to the first using the paired sign test ( $p=.0039$ ). Analysis of the sixteen patients with repeat measurements also found a significant increase in POPQ stage from the first to the third trimesters using the paired t-test ( $p=0.0011$ ). Analysis of the nine individual points that comprise the POPQ was also performed. Significant changes were seen in several of the points, but the most surprising change was observed in point PB, which corresponds to the perineal body measurement. This was found to increase significantly between the first and third trimesters using a paired t-test ( $p<.01$ ). Conclusion: These results likely represent normal physiologic changes of the pelvic floor during pregnancy but suggest that significant changes are present prior to delivery.

### Detail Summary Sheet

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|---|--|--|-----------------------|--------------------------------------|--|
| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 81/035                  |                       | <b>Status:</b> Ongoing               |  |
| <b>Title:</b> GOG 0041: Surgical Staging of Ovarian Carcinoma   |  |  |                       |                                      |  |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN  |  |  |                       |                                      |  |
| <b>Department:</b> OB   |  |  | <b>Facility:</b> MAMC |                                      |  |
| <b>Associate Investigator(s):</b> COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC |  |  |                       |                                      |  |
| <b>Keywords:</b> cancer:ovarian,surgical staging  |  |  |                       |                                      |  |
| <b>Start Date:</b><br>1/16/1981   |  | <b>Est. Completion Date:</b><br>Jan 86 |                       | <b>Periodic Review:</b><br>9/24/2002 |  |

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a completed and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This study closed to patient entry, 12 Feb 87. Thirteen patients were enrolled. Eight patients remain disease free and continued to be followed at MAMC during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 81/105 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

**Title:** GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC; COL Mark E. Potter, MC

**Keywords:** Cancer:ovarian, adenocarcinoma, cyclophosphamide, Adriamycin, Platinol

**Start Date:**  
8/21/1981

**Est. Completion Date:**  
Mar 98

**Periodic Review:**  
9/24/2002

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG 0025.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This study closed to patient entry, 20 Jul 85. Six patients were enrolled. One patient remains disease free after completing therapy, and continued to be followed at MAMC during FY02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 84/033                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease  |  |                                      |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN   |  |                                      |
| <b>Department:</b> OB  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC  |  |                                      |
| <b>Keywords:</b> tumor;ovarian,melphalan,cisplatin   |  |                                      |
| <b>Start Date:</b><br>2/17/1984  | <b>Est. Completion Date:</b><br>Dec 88 | <b>Periodic Review:</b><br>9/24/2002 |
| <b>Study Objective:</b> To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.   |  |                                      |
| <b>Technical Approach:</b> Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for five years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter. |  |                                      |
| <b>Progress:</b> This study closed to patient entry 25 Feb 92. Ten patients were enrolled; of these, 8 patients continued to be followed at MAMC during FY02.  |  |                                      |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 84/074      **Status:** Ongoing

**Title:** GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

**Department:** OB      **Facility:** MAMC

**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

**Keywords:** cancer:ovarian,teratoma,tumor:sinus,chemo,bleomycin,cisplatin

**Start Date:**  
8/17/1984

**Est. Completion Date:**  
Jul 89

**Periodic Review:**  
9/24/2002

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** This study closed to patient entry, 10 Feb 92. One patient continued to be followed at MAMC during FY02 and remains disease-free off-therapy.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 86/089 | <b>Status:</b> Ongoing               |
| <b>Title:</b> GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes  |  |                       |                                      |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN  |  |                       |                                      |
| <b>Department:</b> OB   |  | <b>Facility:</b> MAMC |                                      |
| <b>Associate Investigator(s):</b> COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC; COL Mark E. Potter, MC   |  |                       |                                      |
| <b>Keywords:</b> Cancer:cervical, carcinoma, hydroxyurea, 5-FU, Cisplatin, Radiotherapy   |  |                       |                                      |
| <b>Start Date:</b><br>8/15/1986   | <b>Est. Completion Date:</b><br>Feb 94 |                       | <b>Periodic Review:</b><br>9/24/2002 |
| <b>Study Objective:</b> To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.   |  |                       |                                      |
| <b>Technical Approach:</b> Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years. |  |                       |                                      |
| <b>Progress:</b> This study closed to patient entry, 3 Dec 90. Two patients, disease free after completion of therapy, continued to be followed at MAMC during FY02.  |  |                       |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 87/104 | <b>Status:</b> Ongoing |
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**Title:** GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC; COL Donald H. Kull, MC; COL Mark E. Potter, MC

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**Keywords:** cancer:cervix,hysterectomy,lymphadenectomy,radiotherapy

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**Start Date:**  
8/21/1987

**Est. Completion Date:**  
Indef

**Periodic Review:**  
9/24/2002

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**Study Objective:** To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

**Technical Approach:** All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

**Progress:** This study closed to patient entry, 18 Dec 95. One patient, enrolled in FY 88, remains disease free and continued to be followed at MAMC during FY02.

### Detail Summary Sheet

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|---|---------------------------------------|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 87/028                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAI and IBI and IAII and IBII Ovarian Cancer, Phase III |                                       |                                      |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN  |                                       |                                      |
| <b>Department:</b> OB   |                                       | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC   |                                       |                                      |
| <b>Keywords:</b> cancer:ovarian,cyclophosphamide,cisplatin,P32  |                                       |                                      |
| <b>Start Date:</b><br>11/21/1986  | <b>Est. Completion Date:</b><br>Indef | <b>Periodic Review:</b><br>9/24/2002 |

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAI and IBI patients with poorly differentiated tumors and stage IAII and IBII (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin in patients with ovarian cancer. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m<sup>2</sup> IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This study closed to patient entry, 14 Mar 94. Five patients were enrolled. One patient, who remains disease free, continued to be followed at MAMC during FY02

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 87/091 | <b>Status:</b> Ongoing |
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**Title:** GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

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**Keywords:** cancer:endometrial,radiotherapy

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**Start Date:**

6/19/1987

**Est. Completion Date:**

Indef

**Periodic Review:**

9/24/2002

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**Study Objective:** To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

**Technical Approach:** Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGy in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

**Progress:** This study closed to patient entry, 3 Jul 95. Three patients were enrolled. All are currently clinically disease free and continued to be followed during FY02.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 91/086

**Status:** Ongoing

**Title:** GOG 0109 (SWOG 8797): A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy, versus Radiation Therapy Alone in Selected Patients with Stages I-A2, I-B, and II-A Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** COL Mark E. Potter, MC

**Keywords:** cancer:cervix,5-Fluorouracil,cisplatin,radiotherapy

**Start Date:**  
8/2/1991

**Est. Completion Date:**  
Sep 94

**Periodic Review:**  
9/24/2002

**Study Objective:** To determine whether the combination of 5-fluorouracil (5-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins following radical hysterectomy and lymph node dissection for Stages I-A2, I-B, and II-A carcinoma of the cervix and to determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

**Technical Approach:** Patients must have primary, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, clinical stages I-A2, I-B, or II-A and must have had a radical hysterectomy with total pelvic lymphadenectomy and para-aortic sampling. Patients must have, at surgical evaluation, either histologically confirmed positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins. Patients with confirmed positive para-aortic lymph nodes are not eligible. Patients must not have received prior chemotherapy, immunotherapy (including biologics), hormonal therapy, or pelvic irradiation. Patients will be randomly assigned to receive either 5-FU and cisplatin plus pelvic irradiation or pelvic irradiation alone. Patients with positive high common iliac lymph nodes will receive extended field para-aortic irradiation. Irradiation and chemotherapy will begin simultaneously within six weeks after surgery. Chemotherapy will be given once a week every three weeks for four cycles. Radiation therapy will be given for six weeks. After completion of therapy, patients will be followed every 3 months for two years and every 6 months thereafter. Formal analysis of progression-free and overall survival will be performed at 2 1/2 years after the start of patient accrual to determine if consideration should be given to early termination of either treatment arm.

**Progress:** This study closed to patient entry, 20 May 94. One patient, enrolled in 1991, remains without evidence of recurrence of disease and continued to be followed during FY02.

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 91/074 | <b>Status:</b> Ongoing |
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**Title:** GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, and Unclassified Sex Cord Stromal Tumor)

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** COL Mark E. Potter, MC

**Keywords:** tumor;ovarian stroma,chemo,bleomycin,etoposide,cisplatin

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**Start Date:**

7/12/1991

**Est. Completion Date:**

Indef

**Periodic Review:**

9/24/2002

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**Study Objective:** To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma as a first-line regimen.

**Technical Approach:** Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

**Progress:** This study closed to patient entry, April 1997. One patient had disease detected at second look laparotomy in Sep 98. However, she still has no clinical evidence of disease and continued to be followed during FY02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 93/063                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix   |  |                                      |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN   |  |                                      |
| <b>Department:</b> OB  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> COL Mark E. Potter, MC   |  |                                      |
| <b>Keywords:</b> cancer:cervix, radiation therapy, cisplatin, hysterectomy   |  |                                      |
| <b>Start Date:</b><br>3/5/1993   | <b>Est. Completion Date:</b><br>Oct 97 | <b>Periodic Review:</b><br>9/24/2002 |
| <b>Study Objective:</b> To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.   |  |                                      |
| <b>Technical Approach:</b> This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m <sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens. |  |                                      |
| The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered.   |  |                                      |
| <b>Progress:</b> This study closed to patient entry, April 1997. One patient was enrolled who remains without evidence of recurrence of disease and continued to be followed at MAMC during FY02   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/012 | <b>Status:</b> Ongoing |
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**Title:** SWOG GO182: A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ David E. McCune, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** Cancer:Ovarian cancer, peritoneal carcinoma, paclitaxel, carboplatin

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**Start Date:**  
10/23/2001

**Est. Completion Date:**  
Nov 04

**Periodic Review:**  
11/26/2002

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**Study Objective:** (1) To compare the efficacy of each experimental arm with the control arm (paclitaxel and carboplatin). Efficacy will be determined through analysis of overall survival and progression-free survival, (2) To compare the response rate in patients with measurable disease, toxicities and complications of each treatment regimen and to describe dose-intensity and cumulative dose delivery for each regimen and (3) To extend the accrual into a study initiated with GOG Protocol #0172 which will assess whether inactivated BRCA1 and /or BRCA2 is a prognostic factor for clinical outcome.

**Technical Approach:** This study is designed to compare the effectiveness and side effects of several chemotherapy combinations (Paclitaxel, Carboplatin, Gemcitabine, Topotecan, Doxil [Liposomal Doxorubicin]) which are known to be effective in women with ovarian or primary peritoneal cancer. This study will enroll adult females with histologic diagnosis of primary peritoneal carcinoma or epithelial ovarian carcinoma, Stage III or IV, with either optimal or suboptimal residual disease following initial surgery.

**Progress:** Two patients enrolled in this study 02 and continue on treatment. Patient enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/136                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> SWOG S0009: A Phase II Evaluation of Neoadjuvant Chemotherapy, Interval Debulking Followed by Intraperitoneal Chemotherapy in Women with Stage III and IV Epithelial Ovarian Cancer, Fallopian Tube Cancer or Primary Peritoneal Cancer   |  |                                      |
| <b>Principal Investigator:</b> LCDR John D. O'Boyle, MC, USN  |  |                                      |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ David E. McCune, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC   |  |                                      |
| <b>Keywords:</b> SWOG chemotherapy debulking women intraperitoneal  |  |                                      |
| <b>Start Date:</b><br>9/25/2001   | <b>Est. Completion Date:</b><br>Aug 04 | <b>Periodic Review:</b><br>8/12/2002 |
| <b>Study Objective:</b> (1) To evaluate the overall survival and progression-free survival in Stage III or IV epithelial ovarian, fallopian tube or primary peritoneal carcinoma patients with bulky disease and/or malignant pleural effusions treated with neoadjuvant intravenous paclitaxel and carboplatin, cytoreductive surgery and intravenous/intraperitoneal paclitaxel and intraperitoneal carboplatin, (2) To estimate the percent of patients successfully cytoreduced to optimal disease (<1 cm residual) following neoadjuvant chemotherapy, (3) To evaluate the toxicities associated with this therapy, and (4) To explore the relationship between tumor p53 expression, cellular proliferation rate as measured by PCNA and apoptotic rate, and human tumor cloning assay results at time of debulking surgery with progression-free survival and overall survival in patients undergoing cytoreductive surgery. |  |                                      |
| <b>Technical Approach:</b> This protocol evaluates the effectiveness and side effects of a treatment regimen for advanced ovarian, peritoneal, and fallopian tube cancers. The treatment consists of intravenous chemotherapy of paclitaxel and carboplatin (3 treatments), followed by surgery, followed by a combination of intravenous paclitaxel and intra-peritoneal carboplatin and paclitaxel (6 treatments).  |  |                                      |
| <b>Progress:</b> No subjects enrolled in this study at MAMC during FY02. Subject enrollment continues.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/080 | <b>Status:</b> Ongoing |
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**Title:** SWOG S9701: Phase III Randomized Trial of 12 Months vs. 3 Months of Paclitaxel in Patients With Advanced Ovarian, Fallopian Tube or Primary Peritoneal Cancer who Attain a Clinically Defined Complete Response (CR) Following Platinum/Paclitaxel-Based Chemotherapy

**Principal Investigator:** LCDR John D. O'Boyle, MC, USN

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Inez J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

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**Keywords:** SWOG, Paclitaxel, S9701, progression free survival

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**Start Date:**  
2/27/2001

**Est. Completion Date:**  
Dec 10

**Periodic Review:**  
2/26/2002

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**Study Objective:** To assess whether the continuation of paclitaxel, a cycle specific antineoplastic agent, for 12 months following the attainment of a clinically-defined complete response (CR) to initial platinum (carboplatin or cisplatin)/paclitaxel-based chemotherapy can significantly increase progression-free survival and overall survival when compared to a 3-months continuation in women with advanced ovarian cancer and to assess the toxicities associated with prolonged paclitaxel.

**Technical Approach:** Female patients with histologically confirmed epithelial carcinoma of the ovary, fallopian tube cancer or primary peritoneal cancer. Eligible patients will be randomized to receive paclitaxel (Taxol) once a month for 3 months (3 courses), or once a month for 12 months (12 courses). Patients will be removed from the study if side effects become too severe or in case of disease progression.

**Progress:** Protocol opened 2/27/01, one patient enrolled 4/12/01, then protocol permanently closed 11/1/01. Patient on follow-up.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 201/033

**Status:** Completed

**Title:** Train the Trainers Program: Introduction of Formal Curriculum and Exercise Program for Instructors I Corps/MAMC PSWP

**Principal Investigator:** MAJ Katherine M. Opitz, AN

**Department:** OB

**Facility:** MAMC

**Associate Investigator(s):** MAJ Elizabeth C. Golladay, MC; COL Robert E. Ricks, MC; COL Roderick F. Hume, MC; SGT Steffie Castillo, USA; LCDR Mary G. Battaglia, NC, USNR; CPT Kim Whittington, MC; CPT Sandra L. Hernandez, MC; CPT Melissa V. Terry, MC

**Keywords:** Educational intervention, training, soldiers, physical fitness training for active duty pregnant soldiers, military specific

**Start Date:**

1/23/2001

**Est. Completion Date:**

Sep 01

**Periodic Review:**

11/27/2001

**Study Objective:** Introduction of formal curriculum of education and instructional preparation will enhance the motivation of PSWP participants, increase attendance and improve performance. This is team building and soldier development for an existing mandatory exercise program for active duty pregnant soldiers at Ft. Lewis. Goal is to enhance the training of soldier instructors (PSWP Trainers) and provide teaching aides to facilitate the PSWP.

**Technical Approach:** Formalize the existing training into modern photoimages of exercise program, instructors handbook, and learning aides. Train sets of instructors and monitor attendance, satisfaction and performance (return to fitness) as measures of success.

62nd Med Group Ft. Lewis is primary agent for the Ft. Lewis/I Corps PSWP. MAMC Female Soldier Readiness Group supports with MFM Consultants and weekly PSWP Focus OB Clinics. Training program has been in existence for 16 years as an informal instructional package for the Female Fitness Volunteer Project (BAMC 82-84), (97th Gen Hosp 84-87, Duke University Medical Center - Rational Approach to Exercise During Pregnancy for Postpartum Recovery (87-89), and MAMC (95-present). The PSWP is now entering its 3rd year. The soldiers have requested the opportunity for more formal instruction, certification and support to self-improve the PSWP program. Education interventional trial. Trainers will be instructed formally beginning December 2000. Formal Publication goal for March 2001. Attendance records, formal and informal focus group methodologies will be used for satisfaction, and return to fitness will serve as outcome measures.

**Progress:** This study has been reported as completed and results presented at Armed Forces Day, 2001.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/034 | <b>Status:</b> Ongoing |
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**Title:** Return to Fitness After Implementation of Formal PSWP AD OB Focus Interdisciplinary Clinic and Discharge Education

**Principal Investigator:** COL Robert E. Ricks, MC

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Elizabeth C. Golladay, MC; LCDR Amy L. O'Boyle, MC, USNR; LCDR Mary G. Battaglia, NC, USNR; COL Roderick F. Hume, MC; CPT Kim Whittington, MC; CPT Sandra L. Hernandez, MC; CPT Melissa V. Terry, MC; COL Byron C. Calhoun, MC, USAF; LTC Peter G. Napolitano, MC

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**Keywords:** Soldier training, Educational initiative, unit training, physical training of female soldier, military specific

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**Start Date:**  
1/23/2001

**Est. Completion Date:**  
Nov 01

**Periodic Review:**  
12/4/2002

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**Study Objective:** Focussed Obstetrical care has proven beneficial for teen pregnancy and enlisted pregnant soldiers by our group. We have re-introduced the concept of an interdisciplinary clinic whose focus is the active duty pregnant soldier (servicemember). All AD pregnancies will be offered streamlined access to this clinic for NOB, NOB limited US, Pelvic Floor evaluation, Continuing Obstetrical care, Coordination of Ob Profile and PSWP participation. At Delivery individualized education for postpartum recovery and return to fitness help and return to duty clinics will be coordination specifically addressing the unique challenges facing the new soldier mom.

**Technical Approach:** Re-engineering of existing clinical resources into a focused interdisciplinary team approach to the obstetrical care for soldiers. Educational interventional trial for the impact of the PSWP OB Clinic upon the Ob Outcome and Return to Fitness for soldiers who participate compared to those who do not. ( Historical controls and Non I Corps AD).

**Progress:** PT scores collected and correlated; however numbers are inadequate at present time.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/068                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> The Role of Methergine in the Management of Spontaneous Abortion  |  |                                      |
| <b>Principal Investigator:</b> CPT Jodi L. Schulz, MC   |  |                                      |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC Gregory E Chow, MC; CPT Robert W. Chalmers, MC; CPT Jennifer A. Brown, MC; CPT Sandra L. Hernandez, MC; CPT Kimberly Devore, MC |  |                                      |
| <b>Keywords:</b> methergine, spontaneous abortion, conservative management  |  |                                      |
| <b>Start Date:</b><br>4/25/2000   | <b>Est. Completion Date:</b><br>Mar 01 | <b>Periodic Review:</b><br>4/24/2001 |

**Study Objective:** (1) Comparison of failure rates of conservative therapy in management of spontaneous abortions. Failed conservative management is defined as requiring a dilation and curettage; (2) Amount of blood loss; (3) Duration to completion of spontaneous loss (# days until quantitative BHCG<5); (4) Pain scale (control vs. methergine).

**Technical Approach:** Patients presenting with the clinical and laboratory diagnosis of spontaneous abortion and desiring conservative therapy will be randomized to methergine or placebo treated groups. Each group will be asked to take their medication for 24 hours. On Day #1, laboratory data including CBC and quantitative B-HCG will be obtained. B-HCG values will be followed on Days #4 and #7, then weekly until values are below 5 (indicating uterine evacuation). At this time, a CBC will be evaluated and the patient will complete a pain scale to measure amount of pain associated with the treatment.

**Progress:** A total of ten patients have been enrolled in this study at MAMC. Four patients required D&C, four spontaneously resolved their pregnancy and two patients passed tissue spontaneously but were unwilling to continue the study and were lost to follow-up with no data collected.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/088 | <b>Status:</b> Terminated |
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**Title:** Incidence of Occult External and Internal Anal Sphincter Defects in Patients Presenting with Rectocele

**Principal Investigator:** MAJ Stephen D. Seymour, MC

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| <b>Department:</b> OB | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Ronald J. Place, MC; COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; LCDR Amy L. O'Boyle, MC, USNR

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**Keywords:** anal sphincter, rectocele

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**Start Date:**

3/27/2001

**Est. Completion Date:**

Jun 01

**Periodic Review:**

4/23/2002

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**Study Objective:** To determine the incidence of unrecognized internal and external anal sphincter defects in patients evaluated for rectocele.

**Technical Approach:** Patients will be identified and asked if they desire to participate in the study. A thorough medical history will be obtained with emphasis on anal incontinence. Study participants will undergo thorough physical examination according to the International Continence Society's system for grading pelvic organ prolapse. Patients will then have an endoanal ultrasound performed to determine the status of anal sphincters. Results of the endoanal ultrasound will be evaluated on the basis of the incidence of occult anal sphincter defects in patients found to have a rectocele on examination. This information will then be related to the stage of pelvic organ prolapse, type of anal incontinence if present, gravidity, parity, the number of vaginal deliveries, fetal weights and other factors associated with delivery in an attempt to determine any correlations.

**Progress:** This study was reported as terminated, 29 May 02, due to the PCS of its principal investigator.



### Detail Summary Sheet

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|---|--|--|-----------------------|--------------------------------------|--|
| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 201/067                 |                       | <b>Status:</b> Completed             |  |
| <b>Title:</b> Outcomes of Overlapping Anal Sphincteroplasty in a Military Medical Center  |  |  |                       |                                      |  |
| <b>Principal Investigator:</b> MAJ Stephen D. Seymour, MC   |  |  |                       |                                      |  |
| <b>Department:</b> OB   |  |  | <b>Facility:</b> MAMC |                                      |  |
| <b>Associate Investigator(s):</b> MAJ Patrick J. Woodman, MC; LTC Ronald J. Place, MC; COL George B. McClure, MC; MAJ Andrew Walter, MC, USAF; LCDR Shawn Menefee, MC, USN; Lt Col John R. Fischer, MC, USAF  |  |  |                       |                                      |  |
| <b>Keywords:</b> Overlapping Anal Sphincteroplasty, Anal Repair, Fecal Incontinence, Surgical Outcomes  |  |  |                       |                                      |  |
| <b>Start Date:</b><br>2/27/2001   |  | <b>Est. Completion Date:</b><br>Jan 02 |                       | <b>Periodic Review:</b><br>1/22/2002 |  |
| <b>Study Objective:</b> (1) Review the colorectal surgery literature to determine the patient population pre-operative work-up, efficacy and complications associated with overlapping anal sphincteroplasty (OAS), (2) Comparison of the findings in the above literature review with what is seen in a cohort of patients evaluated in military urogynecology and colorectal practices and (3) Determine if adding OAS to complete, site-specific urogynecologic surgical repair affects outcome of OAS in terms of effectiveness or complications.   |  |  |                       |                                      |  |
| <b>Technical Approach:</b> The investigators have reviewed surgical logs over the investigative period and determined that approximately 60 overlapping sphincteroplasties have been performed at MAMC with or without adjunctive Urogynecologic procedures between 1JUL98 to 30JUN00. These patients' inpatient and outpatient charts will be scrutinized to allow the investigators to fill out patient data sheets. The individual patients that meet inclusionary criteria will be sent a patient questionnaire, starting 1FEB2001 which includes a validated patient symptom and satisfaction questionnaire. If not returned, the questionnaire will be sent again on 1MAR2001. Responders and nonresponders will be compared to determine if there are any differences between the groups. When the questionnaires are returned, the symptom data will be compared to the chart-derived patient data sheets. Step-wise logistical regression will be used to identify factors associated with poor outcome, early and late complications. his will be done for non-responders, Urogynecology and Colorectal primary surgeons, and military branch, as well, to identify any associated factors. |  |  |                       |                                      |  |
| <b>Progress:</b> All data collection for this protocol has been completed. An abstract of findings continues to be pending due to PCS of the principal investigator, MAJ Seymour.   |  |  |                       |                                      |  |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/033                 | <b>Status:</b> Completed |
| <b>Title:</b> Patient Satisfaction and Body Image After Obliterative Procedures for Severe Pelvic Organ Prolapse Across Two Cultures |  |                          |
| <b>Principal Investigator:</b> MAJ Stephen D. Seymour, MC  |  |                          |
| <b>Department:</b> OB  | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> LTC Henry E. Ruiz, MC; COL Gary D. Davis, MC   |  |                          |
| <b>Keywords:</b> Colpocleisis, Colpectomy, Obliterative procedures, Body image, Quality of life                                      |  |                          |
| <b>Start Date:</b><br>2/26/2002  | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b>  |

**Study Objective:** To evaluate cultural differences in patient satisfaction and body image after an obliterative gynecologic procedure.

**Technical Approach:** Madigan Army Medical Center, through the department of Urology accepted a Humanitarian surgical Mission to Honduras, Central America. The division of Urogynecology, Dept. of OB-GYN, was invited to provide an accompanying team to provide urogynecologic care on the mission. During that mission four obliterative procedures were performed. Surgical logs of the lead investigator will be reviewed and all patients who underwent colpocleisis or colpectomy will be mailed a 16 item questionnaire. Responses to the questionnaire will be compiled and evaluated. For the Honduran group, a review of data from the medical records, which included the questions about body image and quality of life, which is offered to all patients undergoing obliterative procedures, will be done This will be compared to responses obtained from an equal number of US women. All patients who have undergone an obliterative vaginal procedure will be given a 16 item questionnaire. For those who underwent the procedure in the US, questionnaires will be returned via an enclosed self-addressed stamped envelope. If no response is received after 4 weeks a second mailing will take place. The data will be evaluated and a comparison will be made between the US and the Honduran group for differences in quality of life, and body image.

**Progress:** All data collection for this protocol has been completed. An abstract of findings continues to be pending due to PCS of the principal investigator, MAJ Stephen Seymour, MC.

## Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/087                 | <b>Status:</b> Completed             |
| <b>Title:</b> Retropubic Urethrolisis for the Management of Post-Urethropey Urinary Retention and Voiding Dysfunction |  |                                      |
| <b>Principal Investigator:</b> MAJ Stephen D. Seymour, MC   |  |                                      |
| <b>Department:</b> OB   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Patrick J. Woodman, MC; LTC Henry E. Ruiz, MC                                   |  |                                      |
| <b>Keywords:</b> Bladder outlet obstruction, urethropey, urethrolisis, voiding dysfunction                            |  |                                      |
| <b>Start Date:</b><br>3/27/2001   | <b>Est. Completion Date:</b><br>Feb 04 | <b>Periodic Review:</b><br>3/21/2002 |

**Study Objective:** To describe objective and subjective symptomatologic and functional improvement in patients undergoing an abdominal approach to urethrolisis, when their obstructing procedure was a retropubic urethropey (such as a Burch or Marshall-Marchetti-Krantz colposuspension). The data derived from our cohort will be compared to historical data published in the literature.

**Technical Approach:** Sequential women meeting selection criteria for partial bladder outlet obstruction with post-operative urinary retention (>100mL PVR), voiding dysfunction, and/or persistent de novo irritative voiding symptoms after urethropey will be considered candidates for the study. Every portion of this study is the current standard of practice at Madigan. The fact that we will be testing people pre- and post-operatively makes this study an outcomes study for scientific merit, but not for human use concerns since we are already doing the following procedures and they are standard practice.

Demographic data will be collected, a comprehensive history and physical performed, as well as obtaining information about the obstructing procedure from the patient. This will be confirmed by retrospective inspection of all in-patient and out-patient notes pertinent to her complaint. A symptom survey will be obtained from the subject. Interventions will be recorded (medications, biofeedback, CISC, previous surgical attempts at urethrolisis).

Pre-surgical evaluation will consist of provocative multi-channel or video urodynamics, voiding pressure study, urethral profilometry, cystourethroscopy voiding diary and symptom questionnaire. If the clinical diagnosis of iatrogenic bladder outlet obstruction is made, the subject will be ask to enroll in the study. Technique of retropubic urethrolisis has been described elsewhere<sup>21</sup>. An omental fat pad, when available, or Seprafilm™ (Genzyme Surgical Products; Cambridge, MA) will be interposed between the urethra and pubic bone, to limit reformation of post-surgical scarring. All patients will be counseled of the possibility that urethral hypermobility could return after urethrolisis.

Post-surgical evaluation will consist of cystourethroscopy, voiding diary, symptom questionnaire and serial post-void residual measurements. Each subject will also be given a patient satisfaction questionnaire (Madigan Urethrolisis Questionnaire (Attachment #2)). This patient satisfaction questionnaire is the only thing that will be done differently when subjects are compared to patients who do not participate in the study. Interval pre- and post-operative variables will be analyzed using the paired-t test.

Symptom/quality-of-life questionnaire (IIQ-7 & UDI-6) data will be analyzed by Wilcoxon signed ranks test. Demographic data and parameters measured either only pre- or only post-operatively will be analyzed by descriptive statistics.

**Progress:** All data collection for this protocol has been completed. An abstract of findings continues to be pending due to PCS of the principal investigator, MAJ Stephen Seymour, MC.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/078 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Interleukin 18 Cord Blood Levels at Delivery in Patients with Preeclampsia

**Principal Investigator:** CPT Melissa V. Terry, MC

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**Department:** OB

**Facility:** MAMC

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**Associate Investigator(s):** LTC Peter G. Napolitano, MC; MAJ Christine M. Kovac, MC; MAJ Bobby C. Howard, MC, USAF

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**Keywords:** Interleukin 18 preeclampsia cord blood

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**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Jun 02

**Periodic Review:**

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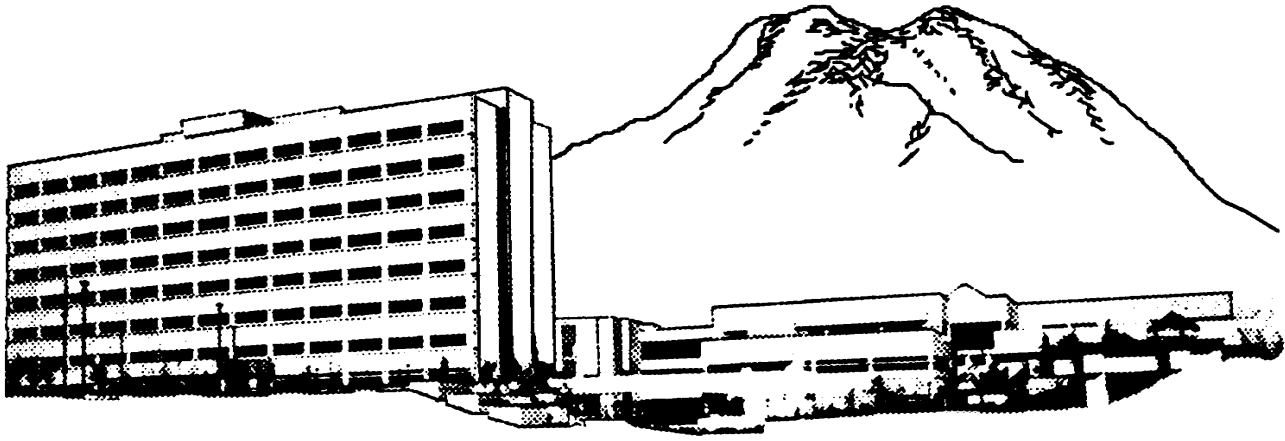
**Study Objective:** To determine baseline umbilical cord blood plasma levels of Interleukin 18 (IL-18) in neonates of women with preeclampsia compared with normal controls.

**Technical Approach:** Once the placenta is discarded, cord blood samples will be collected. Blood serum will be frozen and delivered to DCI for analysis. Interleukin 18 (IL-18) levels will be measured by DCI lab staff who are blind to which samples are from normal vs. preeclamptic placentae.

**Progress:** Umbilical cord blood samples from 15 control subjects and 15 study subjects have been obtained and are currently in storage in DCI. The IL-18 assay kits have been ordered. The bench work will be completed upon arrival of the assay kits. Patient care was not affected by sample collection.

### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/106                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> MAMC Clinical Investigation Protocol: The Evaluation of Procedural Skills in the Repair of Episiotomy and Obstetrical Lacerations  |  |                                      |
| <b>Principal Investigator:</b> MAJ Geoffrey D. Towers, MC  |  |                                      |
| <b>Department:</b> OB  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> COL Gary D. Davis, MC; COL Robert E. Ricks, MC; LTC Peter E. Nielsen, MC; COL George B. McClure, MC; LCDR John D. O'Boyle, MC, USN; MAJ Stephen D. Seymour, MC; LCDR Amy L. O'Boyle, MC, USNR  |  |                                      |
| <b>Keywords:</b> Obstetrical Lacerations, Episiotomy, Repair   |  |                                      |
| <b>Start Date:</b><br>6/26/2001  | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b><br>7/11/2002 |
| <b>Study Objective:</b> To evaluate the progress of Residents and Fellows in the practical repair of obstetrical lacerations by an objective Cumulative Sum Analysis (CUSUM), and to determine the number of repairs needed to attain competence.  |  |                                      |
| <b>Technical Approach:</b> Fifty patients at Madigan Army Medical Center who have sustained third or fourth degree obstetrical lacerations will be asked to participate in the study. Second year residents will be instructed in the repair of these lacerations by senior faculty who will critique the residents technique according to protocol. Residents will be given a Cumulative Sum Analysis Score (CUSUM) at the conclusion of each R2 year, or the end of the study period. The number of repairs required to achieve acceptable performance as indicated by the CUSCM score will be tabulated for each resident. All subjects will be given detailed pelvic floor evaluation at their six weeks follow up evaluation to include Pelvic Organ Prolapse Quantification (POPQ) scoring, symptom score and evaluation of and sphincter integrity by transaral sonography. Residents will be given feed back from their examinations as to the integrity of their repairs. |  |                                      |
| <b>Progress:</b> No progress has been made on this protocol. The new PI, Dr. Towers, will start it later this year.  |  |                                      |



**Detail Summary Sheets**

**Department of Pathology**

### Detail Summary Sheet

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|--|--|--------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/081                 | <b>Status:</b> Completed |
| <b>Title:</b> Establishing a Lower Reference Range for MAMC Core Laboratory Cardiac Troponin I |  |                          |
| <b>Principal Investigator:</b> CPT Jude Abadie, MS   |  |                          |
| <b>Department:</b> Pathology   | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> MAJ Dale T. Waldner, MC                                      |  |                          |
| <b>Keywords:</b> establishing lower reference range cardiac troponin                           |  |                          |
| <b>Start Date:</b><br>6/25/2002  | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b>  |

**Study Objective:** To establish a lower limit normal reference range for Pathology's cardiac troponin I (cTnI) assay.

**Technical Approach:** This study will utilize a total of 60 men and women of different age ranges who do not have CVD or a history of CVD. We hypothesize that this group will have cTnI values between 0.3 and 1.0 ng/mL, inclusively. This group of subjects will be used to establish a reference range for our cTnI Laboratory assay. Establishing reference ranges for laboratory tests is a necessary part of clinical chemistry practice. This study will establish a negative cTnI reference range for our population of patients at MAMC. This lower limit reference range that we establish in the CVD-free individuals will be used as a guide to limit the number of patients admitted and treated for myocardial infarction who are not experiencing a cardiovascular event. This reference range will be used as a tool to save money, make better use of health care provider time, and most importantly, improve patient care. The American College of Cardiology states that reference values must be determined in each laboratory by studies using specific assays with appropriate quality control, as reported in peer-reviewed journals. Furthermore, each individual laboratory should confirm the range of reference values in their specific setting.

**Progress:** A total of 54 participants enrolled in this study. There were an equal number of males and females. The age range was 19-64. All tests were <0.3 ng/mL except for 2 of them. One of these was from a 44 year woman with a result of 0.8 ng/mL (negative). The other test that was above 0.3 ng/mL was from a 46 year old man with a result of 1.4 ng/mL (negative). Greater than 2.0 ng/mL is positive. This participant, however, had the test re-run at his clinic, and it was negative. A summary of these results is pending.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/132 | <b>Status:</b> Completed |
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**Title:** Methylmalonic Acid (MMA) Level in Serum of Normal population: Important Diagnostic Tool for Evaluation of Cobalamin (Vitamin B12) Deficiency at Tissue Level

**Principal Investigator:** LTC David K. Turgeon, MC

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| <b>Department:</b> Pathology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT Ileana Hauge, USAF; Mark Wener, MD; COL Jerome B. Myers, MC

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**Keywords:** Methylmalonic acid (MMA), Cobalamin

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**Start Date:**

9/25/2001

**Est. Completion Date:**

Nov 01

**Periodic Review:**

9/23/2002

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**Study Objective:** Evaluate MMA serum levels in a normal female population by GC/Mass/Spec. Compare these results to breast cancer patients positive for CA27-CA29 markers that have had their MMA levels measured by standard ELISA techniques.

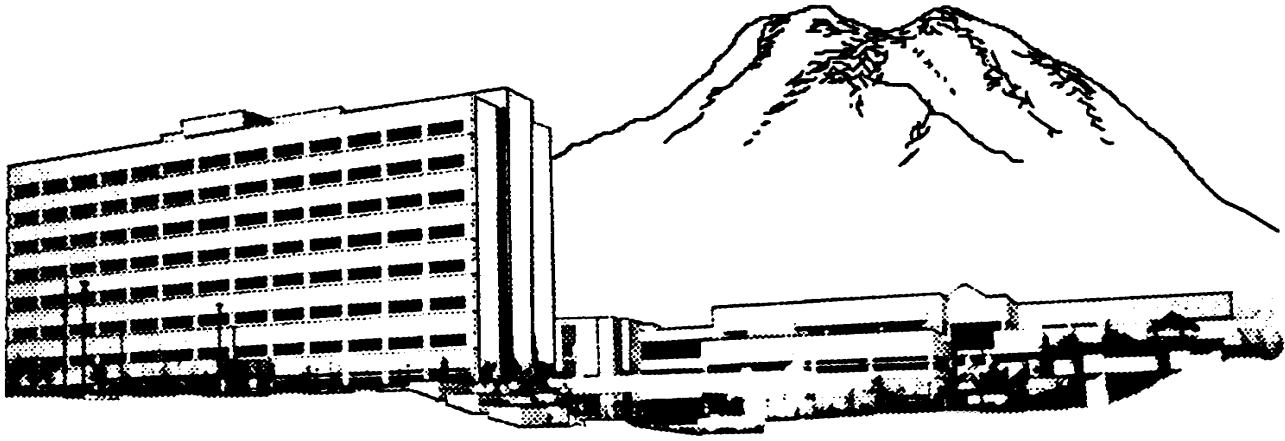
**Technical Approach:** In this study only the gender (females, for example) and the age group (35-45 year old female population, for example) will be included. Frozen serum leftovers, previously tested for breast cancer tumor markers CA27-CA29 from the Immunology laboratory at the University of Washington in Seattle, will be tested for the MMA level in the same manner. Results obtained from the random normal population study will be compared with the results from the CA27-CA29 random population to see if there is any major difference between the two groups. Because methylmalonic acid is a validated indicator of tissue level of vitamin B12, the high CA27-CA29 results should test high for MMA. This study expects to obtain higher levels of MMA in the CA27-CA29 population than the normal random one. The serum samples will be tested only after the method is validated as acceptable at the University of Washington Medical Center, Seattle, WA.

**Progress:** Data collection has been completed; however a final abstract is not yet available.



## Detail Summary Sheet

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|--|--|--------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/036                 | <b>Status:</b> Completed |
| <b>Title:</b> Clinicopathologic Correlation of Celiac Disease Patient Subsets Based on Small Bowel Mucosal T-cell Phenotype  |  |                          |
| <b>Principal Investigator:</b> CPT Jeffrey A. Vos, MC  |  |                          |
| <b>Department:</b> Pathology   | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> James E. Coad, M.D.; LTC Mark D. Brissette, MC; CPT Michael Piesman, MC; COL Jerome B. Myers, MC   |  |                          |
| <b>Keywords:</b> Celiac Disease, Refractory Sprue, Gluten Sensitivity, Intraepithelial Lymphocytes, T-cell Lymphoma  |  |                          |
| <b>Start Date:</b><br>2/26/2002  | <b>Est. Completion Date:</b><br>Oct 02 | <b>Periodic Review:</b>  |
| <b>Study Objective:</b> To determine if phenotypic variations in the lymphoid tissue of small bowel biopsies of celiac patients correlate with differences in clinical course or specific histologic features  |  |                          |
| <b>Technical Approach:</b> The biopsies of a diverse population of patients with celiac disease were previously phenotyped by immunohistochemical methods and subdivided according to the T-cell receptor and CD4/CD8 marker profiles. The clinical histories of these 23 patients with particular attention to their presentation, response to gluten free diet, and overall clinical course will be collected through medical chart and convenience file searches. This data will then be analyzed to determine if any significant relationship can be drawn between the T-cell phenotype and recurring clinical presentation or outcome. Demographic information, associated diseases, complications, and laboratory studies related to celiac disease will also be studied if available. Routine histologic examination has been the mainstay of diagnosing and assessing efficacy of therapy for celiac patients. For this reason, and to validate the findings of other investigators, each biopsy will also be assessed and scored according to a rigorous histologic grading system comprised of architectural, epithelial, and lamina propria changes. These data, in turn, will be analyzed with respect to their phenotypic subgroup to determine if severity of the pathologic findings or if particular histologic features predict clinical outcome or response to therapy. If a correlation exist between the clinical and phenotypic data, then the determination of T-cell profile at the initial diagnosis of the disease may lead to improved therapeutic management and may have prognostic implications. Moreover, these studies may lead to a better understanding of the pathogenesis of celiac disease and propensity for devastating complications. |  |                          |
| <b>Progress:</b> IHC analysis showed 3 distinct phenotypic groups. Fourteen patients (60.9%) had a classic CD phenotype (elevated CD4-CD8- T-cells), 5 patients (21.7%) had T-lymphocytic subsets identical to the normal controls, and 4 patients (17.4%) exhibited a variant profile (elevated CD4-CD8-T-cells). Comprehensive histologic assessment demonstrated near perfect interobserver reliability (Cohen's $\kappa=0.87$ , when agreement = + 1.5 points); however, no morphologic features were indicative of clinical response or phenotypic subgrouping. Architectural distortion and focal gland drop-out were the only histologic features seen more often in the non-classic CD groups (66.7% vs. 28.6%). Review of the clinical data showed no significant discriminators predictive of response to GFD including age at presentation, symptomatology, laboratory studies, or associated diseases. Among the cases phenotypically identified as classic CD, 84.6% exhibited complete and sustained resolution of clinical symptoms while on GFD. Conversely, 75% of those with non-classic CD phenotype showed either only a partial response or no response to GFD. Conclusions: The histologic and clinical criteria in this study did not accurately predict response to GFD in CD. While patients with normal or variant phenotype expressions may show minimal or complete absence of sustained response to GFD, the vast majority of patients with a classic CD phenotype exhibited clinically significant long-term response to therapy.  |  |                          |



**Detail Summary Sheets**

**Department of Pediatrics**

## Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/077                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> ECHO-Pac Electronic Children's Hospital of the Pacific PacRim Consult Trial |  |                         |
| <b>Principal Investigator:</b> COL David T. Estroff, MC                                   |  |                         |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> COL Charles W. Callahan, MC; Francis Malone, MD         |  |                         |
| <b>Keywords:</b> telemedicine pediatric consultation primary care                         |  |                         |
| <b>Start Date:</b><br>6/25/2002   | <b>Est. Completion Date:</b><br>May 04 | <b>Periodic Review:</b> |

**Study Objective:** To evaluate the impact on quality, access and cost of a 12-month period of telemedicine involvement by pediatric subspecialists in care delivered by primary care providers

**Technical Approach:** Referring providers will have access to ECHO-Pac through personal computers with broad-band Internet access. Peripherals will include a digital camera with still and motion-picture capability and flat-bed scanners. They will be able to attach digital images, MPEGs, radiographs and EKGs to the consult information. Referring physicians will enter free-text clinical information about their patients to a secure, encrypted web-site. They will attach digital images as appropriate and submit the consult. Once the consult is submitted, the consult-manager at Tripler will receive an e-mail notification for the new consult. The consult manager will access the web-site, review the consult, then forward it to the appropriate subspecialist. The consultant will then receive an e-mail message requesting his or her assistance with the consult. A hot link will be included in the message to simplify the consultant's access to the case. Once the consultant replies to the consult, the referring physician will receive an e-mail notification to review the consultant's recommendations. In most cases, the referring physician will receive the opinion of a pediatric subspecialist within twenty-four hours of submitting the consult, a major feat in our theater where as many as six time-zones separate Tripler and the primary care site. All consults will be referred to the appropriate consultants and the response time of the consultant will be monitored. With these measures, we will be able to qualify the acceptance of this technology by a population of referring physicians and consultants who have limited exposure to telemedicine. This information should provide valuable insights regarding the acceptance and proliferation of telemedicine technologies across the AMEDD.

**Progress:** As of this date (17 October 02), the project has not formally begun operation here at MAMC. Final approvals and reviews are taking place at the participating facilities. Hardware has started arriving here to set up a dedicated workstation for this project. Next step will be enrolling all relevant consulting specialists here so that they can start responding to consult requests. No research data has been gathered to date. I anticipate that we will be in operation by the end of October 02 or shortly thereafter.

### Detail Summary Sheet

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|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 90/092 | <b>Status:</b> Ongoing |
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**Title:** Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

**Principal Investigator:** LTC Mary P. Fairchok, MC

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| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL James S. Rawlings, MC; MAJ Thomas A. Perkins, MC; LTC Joanna C. Beachy, MC; COL Marvin S. Krober, MC

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**Keywords:** HIV, diagnostic assays, children

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**Start Date:**

7/20/1990

**Est. Completion Date:**

Sep 91

**Periodic Review:**

6/7/2002

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**Study Objective:** To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

**Technical Approach:** Technical Approach: This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children. This analysis will be done in 120-150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

**Progress:** No patients enrolled within the last year. Study remains open for possible enrollment.

### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/142                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model  |  |                         |
| <b>Principal Investigator:</b> LTC Mary P. Fairchok, MC   |  |                         |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> None.   |  |                         |
| <b>Keywords:</b> Pediatric Intubation training Utilizing the Ferret (mustela putorius furo) Model   |  |                         |
| <b>Start Date:</b><br>12/6/2000   | <b>Est. Completion Date:</b><br>Dec 03 | <b>Periodic Review:</b> |
| <p><b>Study Objective:</b> This is a training protocol using a ferret model to teach physicians and other health care professions how to endotracheally intubate (i.e. place a plastic tube in the windpipe) neonates and infants.</p> <p><b>Technical Approach:</b> This training is part of a two-day course in pediatric life-saving techniques; the class is called Pediatric Advanced Life Support(PALS) and is developed by the American Heart Association. PALS is offered through the Department of Emergency Medicine two to four times a year. Students will complete classroom instruction in principles and techniques of pediatric life support. The students will then practice techniques, include endotracheal intubation, on mannequins. Following this practice, students will intubate an anesthetized ferret, which more closely simulates the respiratory anatomy and reflexes of a human child than does a mannequin. Up to six ferrets will be used for each training session and each ferret will serve to train four physicians or other health care providers. The ferrets will be fully anesthetized and will experience no pain during the procedure; they will be closely monitored and observed by a member of the veterinary staff. During the procedure, each of the course participants will learn to place a small plastic tube through the mouth and into the trachea (windpipe) of an anesthetized ferret with the assistance of a small, lighted metal blade called a laryngoscope. The investigators, other course instructors, and veterinary staff will directly supervise the procedure. If any ferret is traumatized or shows signs of problems with the anesthetic drugs, the procedure will be stopped on that animal. No animal will undergo more than seven intubation attempts. After the training session is complete, the animals will be allowed to wake up from anesthesia and will be returned to their usual housing at the MAMC Animal Facility. In the first days following the procedure, the ferrets may experience a mild sore throat, and they will be offered moist food as needed. Ferrets will be housed and maintained according to standard animal husbandry protocols.</p> <p><b>Progress:</b> Pediatric intubation training courses using the resident ferret colony occurred on a quarterly basis. The new PI is Dr Robert Puntel.</p> |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/139 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study

**Principal Investigator:** COL Kelly J. Faucette, MC

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| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Robert G. Irwin, MC

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**Keywords:** Cancer:disseminated lymphoblastic lymphoma, localized lymphoblastic lymphoma, Phase III Intergroup, Pediatric Oncology Group, Childrens Cancer Group,

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**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Sep 07

**Periodic Review:**  
8/8/2002

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**Study Objective:** (1) To compare the event free survival and survival in patients with disseminated lymphoblastic lymphoma treated on four regimens. (NHL/BFM-95 vs. CCG BFM), (2) To determine if treatment with a regimen without high dose methotrexate will maintain the same excellent disease free survival obtained with NHL/BFM-90, (3) To determine if intensification with anthracycline and cyclophosphamide improves disease free survival, (4) To collect outcome data on uniformly treated patients with localized disease or CNS positive disease, and (5) To determine if rapid reduction in tumor volume as defined by chest radiography and CT is predictive of improved outcome.

**Technical Approach:** Patients with disseminated (Murphy stage III or IV) lymphoblastic lymphoma without evidence of CNS disease will be randomized to one of four treatment regimens: Standard CCG BFM (regimen A1); CCG BFM intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen A2); Standard NHL/BFM-95 (regimen B1); or NHL/BFM-95 intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen B2). Patients with disseminated lymphoblastic lymphoma positive for CNS disease will be assigned to the intensified NHL/BFM-95 arm (regimen B2) with delayed radiation therapy. Patients with localized lymphoblastic lymphoma (Murphy stage I or II) will be assigned to the standard CCG BFM arm without additional intrathecal methotrexate (regimen AO). The duration of each treatment arm is 2 years and consists of Induction, Consolidation, Interim Maintenance, Delayed Intensification, and Maintenance therapies.

**Progress:** No patients enrolled in this study at MAMC during FY02. Subject enrollment continues.

### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/109                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> COG AEWS0031-Trial of Chemotherapy Intensification Through Interval Compression in Ewing Sarcoma and Related Tumors, A Phase III Groupwide Study |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC  |  |                                      |
| <b>Keywords:</b> Cancer:Ewing's Sarcoma, intensification chemotherapy, pediatric cancer  |  |                                      |
| <b>Start Date:</b><br>6/26/2001  | <b>Est. Completion Date:</b><br>Jun 07 | <b>Periodic Review:</b><br>8/12/2002 |

**Study Objective:** (1) To determine the effect of chemotherapy intensification using interval compression on event-free survival and survival in children and young adults with Ewing sarcomas and related tumors (Ewing family of tumors), (2) Through linked biology studies, to prospectively assess the prognostic importance of the rearrangement of the EWS gene on chromosome 22, and the presence of RT-PCR evidence of submicroscopic tumor cells in bone marrow and/or peripheral blood at diagnosis and (3) To generate additional hypotheses relating tumor biological characteristics to clinical features that could be tested in future clinical trials.

**Technical Approach:** This is a randomized controlled study to determine whether chemotherapy intensification by reduction of the intervals between chemotherapy cycles can improve the effectiveness of treatment for Ewing sarcoma and related tumors in children, adolescents, and adults. All patients receive chemotherapy with alternating cycles of vincristine-doxorubicin-cyclophosphamide and ifosfamide-etoposide, with G-CSF (filgrastim) between cycles. Patients in the control arm (Regimen A) will start chemotherapy cycles every 21 days, while patients in the experimental arm (Regimen B) will start cycles every 14 days, or as soon as blood counts have recovered. Primary tumor treatment by surgery, radiation, or a combination will begin at week 13, after four cycles of chemotherapy in Regimen A and six cycles in Regimen B. This study expects to enroll 528 patients nationwide with localized tumors over 4-5 years. Analyses of the study will include assessments of event-free survival and survival, toxicity, the degree of intensification achieved in Regimen B, and the relationship between intensification achieved and outcome.

**Progress:** One patient enrolled in this study at MAMC during FY02. Subject enrollment continues.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/108 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** COG ANBL00B1, Neuroblastoma Biology Studies

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer: Biology study, neuroblastoma, tumor tissue, pediatric cancer

**Start Date:**  
6/26/2001

**Est. Completion Date:**  
May 07

**Periodic Review:**  
7/16/2002

**Study Objective:** (1) To prospectively analyze the factors that are currently used for risk-group assignment (DNA content by flow cytometry, MYCN copy number by FISH, and tumor histology using the International Neuroblastoma Pathologic Classification System) in neuroblastoma tumors at the time of diagnosis, (2) to maintain a reference bank containing clinically and genetically characterized frozen tumor tissue, tumor DNA and RNA, tumor touch preparations, histology slides and blocks, cell lines, and paired normal DNA obtained at the time of diagnosis (all patients), at the time of second-look surgery (high-risk patients), and relapse (all patients) for future research studies, (3) to prospectively analyze the prevalence of 1p, 11q, 14q LOH and gain of 17q; the expression of nerve growth factor (NGF) and its high affinity (Trk-A) and low affinity (p75 NTR) receptors; and telomerase activity in diagnostic neuroblastoma tumors, and to determine the independent clinical significance of these biologic factors compared to MYCN amplification, INSS stage, age, and histologic variables in predicting either response to treatment or outcome, and (4) to build a database of the known biologic prognostic factors for patients on therapeutic studies. Adjustment for, or stratification by, these prognostic factors will be performed when testing for treatment effect in Phase III trials.

**Technical Approach:** Clinical and biological factors have been shown to have prognostic value in neuroblastoma. Current therapeutic studies for neuroblastoma patients are tailored according to patient risk. In the Children's Oncology Group (COG), risk-group assignment is currently based on INSS stage, age, MYCN copy number, tumor cell ploidy, and Shimada tumor histopathology. However, additional factors have also been shown to have prognostic value including the level of Trk-A expression, multi-drug resistance associated protein (MRP) expression, telomerase activity, CD44 expression, and genetic abnormalities including LOH of 1p, 11q, 14q and gain of 17q. We hypothesize that analyzing additional genetic and biologic factors will result in a further refinement of the current COG risk-group schema, and will, thereby, impact future risk-based approaches to therapy. We further hypothesize that maintaining tumor and nucleic acid banks with well characterized samples will provide invaluable biologic resources for future research studies that will lead to a further understanding of neuroblastoma biology and the development of new, effective therapy for high-risk patients.

**Progress:** One patient enrolled in this study at MAMC during FY01, no patients enrolled during FY02. Subject enrollment continues.



### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/063                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> COG ANBL00P2 Perinatal Neuroblastoma: Expectant Observation (Observational and Non-Observational Arm) |  |                         |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                         |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                         |
| <b>Keywords:</b> perinatal neuroblastoma expectant observation  |  |                         |
| <b>Start Date:</b><br>4/23/2002   | <b>Est. Completion Date:</b><br>Jul 06 | <b>Periodic Review:</b> |

**Study Objective:** To determine whether non-operative management of adrenal masses found on prenatal and/or neonatal imaging will result in a 3-year patient survival rate of 95%. To estimate the percentage of patients with such masses who are spared resection. To describe the natural and histology of perinatal adrenal masses. To define the tumor biology and histology of prenatal and neonatal neuroblastoma. To attempt to define tumor characteristics that are associated with a need for resection.

**Technical Approach:** In this protocol, infants with small adrenal masses clinically consistent with Stage 1 neuroblastoma will be treated with close observation rather than immediate surgical resection. It is anticipated that a substantial proportion of these adrenal masses will regress in size and disappear in the dcourse of the study. Infants whose masses resolve in this manner will be spared surgery.

**Progress:** This study has not yet been initiated at MAMC pending completion of the IRB approval process.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/054 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** COG P9934: Systemic Chemotherapy, Second Look Surgery and Conformal Radiation Therapy Limited to the Posterior Fossa and Primary Site for Children > 8 Months and < 3 Years with Non-metastatic Medulloblastoma - A Children's Oncology Group Phase III Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC; LTC William B. Reece, MC; COL John D. Werschkul, MC

**Keywords:** Cancer:medulloblastoma, Children's Oncology Group, Phase III, radiation therapy, chemotherapy, pediatric cancer

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**Start Date:**

1/23/2001

**Est. Completion Date:**

Jan 06

**Periodic Review:**

7/15/2002

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**Study Objective:** (1) To determine if the proposed treatment for children > 8.0 months and < 3 years of age at registration with non-metastatic (M0) medulloblastoma is more effective than the combined treatments given to children of the same age and extent of disease on POG 9233, as measured by event-free survival (EFS) rates, (2) to assess the feasibility and safety of the planned use of second look surgery and focal conformal radiation therapy following chemotherapy, (3) to determine the acute and chronic toxicities associated with the above treatment regimens, (4) to describe the neuropsychological and neuroendocrine effects of this systemic chemotherapy, surgery, and local, conformal radiation, (5) to determine the feasibility and validity of a centralized telephone interview based data collection method for neuropsychological evaluations, and (6) to determine the incidence of atypical teratoid/rhabdoid tumor (AT/RT) in children enrolled on this study.

**Technical Approach:** In this study for young children with relatively low risk medulloblastoma, we will test a new therapeutic approach which begins with maximal safe tumor resection and a 16-week, 4-drug induction chemotherapy regimen of cyclophosphamide, vincristine, cisplatin, and oral etoposide. In comparison to the chemotherapy regimens of studies 8633 and 9233, cisplatin is introduced earlier, and given concurrently with the other agents. As well, etoposide is given in an oral form. Based upon the compelling data that outcome is clearly linked to a complete surgical resection the proposed therapy includes a 'second look' surgery following induction chemotherapy in an attempt to resect residual disease in those patients who have failed to achieve a complete response to chemotherapy. To improve local control rates this clinical trial will test the use of conformal radiation therapy and will determine if these techniques can reduce radiation-related side effects. Following recovery from the initial phase of treatment, patients will receive a maintenance phase of chemotherapy, using cyclophosphamide, vincristine, and the prolonged administration of oral etoposide, to complete one year of therapy.

**Progress:** No patients have enrolled onto this study at MAMC. This study remains ongoing for possible patient enrollment.

## Detail Summary Sheet

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|---|--|--|--|--------------------------------------|--|
| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 201/023                 |  | <b>Status:</b> Ongoing               |  |
| <b>Title:</b> COG P9963: A Phase II Trial of Rebeccamycin Analogue (NSC #655649) in Children with Solid Tumors, A COG Phase II Study  |  |  |  |                                      |  |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |  |  |                                      |  |
| <b>Department:</b> Pediatrics   |  |  |  | <b>Facility:</b> MAMC                |  |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |  |  |                                      |  |
| <b>Keywords:</b> Cancer:refractory neuroblastoma, refractory bone sarcomas, refractory soft tissue sarcomas, non-Hodgkin's lymphoma, brain tumors, pediatric cancer   |  |  |  |                                      |  |
| <b>Start Date:</b><br>11/28/2000  |  | <b>Est. Completion Date:</b><br>Nov 03 |  | <b>Periodic Review:</b><br>12/2/2002 |  |
| <b>Study Objective:</b> Primary Objective: (1) To determine if the proposed treatment for children > 8. months and < 3 years of age at registration with non-metastatic (M0) medulloblastoma is more effective than the combined treatments given to children of the same age and extent of disease on POG 9233, as measured by event-free survival (EFS) rates. Secondary Objectives: (2) To assess the feasibility and safety of the planned use of second look surgery and focal conformal radiation therapy following chemotherapy , (3) to determine the acute and chronic toxicities associated with the above treatment regimens, (4) to describe the neuropsychological and neuroendocrine effects of this systemic chemotherapy, surgery, and local, conformal radiation, (5) to determine the feasibility and validity of a centralized telephone interview based data collection method for neuropsychological evaluations and (6) to determine the incidence of atypical teratoid/rhabdoid tumor (AT/RT) in children enrolled on this study.  |  |  |  |                                      |  |
| <b>Technical Approach:</b> This study for young children with relatively low risk medulloblastoma will test a new therapeutic approach. This is designed to (1) increase the disease control rate at 12 months from registration on study by introducing potential surgery and radiation therapy for local disease after four months of systemic chemotherapy, and (2) decrease the early failure rate of chemotherapy utilizing a new schedule of known effective agents. The approach begins with maximal safe tumor resection and a 16-week, 4-drug induction chemotherapy regimen of cyclophosphamide, vincristine, cisplatin, and oral etoposide. In comparison to the chemotherapy regimens of studies 8633 and 9233, cisplatin is introduced earlier, and given concurrently with the other agents. As well, etoposide is given in an oral form. Based upon the compelling data that outcome is clearly linked to a complete surgical resection the proposed therapy includes a 'second look' surgery following induction chemotherapy in an attempt to resect residual disease in those patients who have failed to achieve a complete response to chemotherapy. To improve local control rates this clinical trial will test the use of conformal radiation therapy and will determine if these techniques can reduce radiation-related side effects. Following recovery from the initial phase of treatment, patients will receive a maintenance phase of chemotherapy, using cyclophosphamide, vincristine, and the prolonged administration of oral etoposide, to complete one year of therapy. |  |  |  |                                      |  |
| <b>Progress:</b> One subject enrolled in this study at MAMC, Oct 01; but was subsequently withdrawn, Jan 02, due to progressive disease. The study temporarily closed by C.O.G, 12 Jul 02 ,due to Children's Oncology Group's failure to provide sufficient documentation that: (1) the clinical trials database accurately reflects the data submitted by the treating institution so that accurate response and toxicity reports can be made to CTEP; and (2) adequate procedures are in place for monitoring the study. As such, additional patients will not be enrolled unless C.O.G. reopens the study.   |  |  |  |                                      |  |

### Detail Summary Sheet

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|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 97/145 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

**Title:** D9602: Actinomycin D and Vincristine with or without Cyclophosphamide and Radiation Therapy, for Newly Diagnosed Patients with Low-Risk Embryonal/Botryoid Rhabdomyosarcoma: An IRS-V/STS Protocol

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:rhabdomyosarcoma, cancer:undifferentiated sarcoma, pediatric, actinomycin D, vincristine, radiation therapy

**Start Date:**

9/19/1997

**Est. Completion Date:**

Jul 03

**Periodic Review:**

7/16/2002

**Study Objective:** (1) Treatment of IRS-V low-risk patients with actinomycin D (AMD) and vincristine (VCR), plus local radiotherapy (XRT) for microscopic or gross residual tumor, will result in a failure-free survival rate of 88% at 2 years and an overall survival rate of about 95% at 5 years from initial diagnosis, (2) Treatment of IR8-V low-risk patients with alveolar rhabdomyosarcoma or undifferentiated sarcoma with vincristine and actinomycin D plus cyclophosphamide (collectively called VAC) will result in a failure-free survival rate of greater than or equal to 70% at two years and an overall survival rate of about 80-90% at 5 years, and (3) Reduction in radiation therapy dose for patients with Clinical Group II disease to 36 Gy (from 41.3 Gy) and for Group III patients with orbital disease to 45 Gy (from 50-55 Gy) will result in local control rates of about 90%.

**Technical Approach:** Patients in Group I have no residual tumor following surgery and will receive no radiation therapy. Patients in Group II have microscopic residual tumor and will receive radiation therapy at a dose lower than the current standard. Patients in Group III, orbit tumor only, have visible residual tumor after biopsy and will receive radiation therapy. The results will be compared to current intergroup rhabdomyosarcoma study results. All patients will begin chemotherapy with the two-drug combination of vincristine and actinomycin D, given over a 3-week period while their tumor specimen is being classified at the IRS Group Pathology Center in Columbus, Ohio. Patients whose tumor is classified as embryonal or botryoid rhabdomyosarcoma will continue to receive vincristine and actinomycin D, given at weeks 12 through 21, 24 through 33, and 36 through 45. Patients whose tumor is classified as alveolar rhabdomyosarcoma or undifferentiated sarcoma will have the chemotherapy drug cyclophosphamide added to the combination of vincristine and actinomycin D, given at weeks 3, 6, 9, 12, 15, 18, 24, 27, 30, 36, and 42. Cyclophosphamide will be added on Week 0 for these patients who show molecular genetic or cytogenetic evidence of the t(2;13) or t(1;13) translocation, or the PAX 3-FRHR or PAX 7-FRER gene fusion product.

**Progress:** Enrollment to the protocol is currently suspended by the C.O.G. pending emergent change of therapy for those patients on VAC. No subjects enrolled in this study at MAMC in FY01.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/051

**Status:** Ongoing

**Title:** D9802: A Phase II "Up-Front Window Study" of Irinotecan (CPT-11) Combined with Vincristine Followed by Multimodal, Multiagent Therapy for Selected Children and Adolescents with Newly Diagnosed Stage 4/Clinical Group IV Rhabdomyosarcoma, An IRS-V Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:rhabdomyosarcoma, stage 4 rhabdo, clinical group 4 rhabdo, irinotecan, pediatric cancer

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Feb 06

**Periodic Review:**  
12/18/2001

**Study Objective:** (1) To estimate the response rate associated with two cycles of irinotecan when administered as up-front window therapy, using a low-dose protracted intravenous schedule in high-risk, previously untreated children with metastatic rhabdomyosarcoma, (2) To describe the toxicities associated with irinotecan when administered as described in 1, (3) To describe the toxicities of a new drug pair, vincristine and irinotecan, when given in alternating cycles with vincristine, actinomycin D, and cyclophosphamide (VAC) during continuation therapy in patients who achieve a partial or complete response to the irinotecan window, (4) To estimate the overall and failure-free survival of children with metastatic rhabdomyosarcoma treated with irinotecan followed by VAC alone or VAC alternating with vincristine and irinotecan plus radiotherapy, (5) To study the pharmacokinetics of irinotecan in previously untreated children with rhabdomyosarcoma who are treated on a low-dose, protracted course and who also receive vincristine, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by as positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

**Technical Approach:** Patients with embryonal histology greater than or equal to 10 years of age or alveolar histology (any age) who have stage 4 tumors and who do not have evidence of intracranial extension, base of skull erosion or cranial nerve palsy will be eligible to receive the two cycles of irinotecan as up-front window therapy prior to receiving the standard therapy, Vincristine, Actinomycin D, Cyclophosphamide (VAC), radiotherapy will begin at week 15. Patients with evidence of base of skull erosion or cranial nerve palsy will receive VAC alone and will begin radiotherapy at week 15. Patients with evidence of intracranial extension will receive VAC alone and begin radiotherapy at day 0.

**Progress:** No patients enrolled in this study in FY02 at MAMC. Subject enrollment continues.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/052 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** D9803: Randomized Study of Vincristine, Actinomycin-D, and Cyclophosphamide (VAC) versus VAC Alternating with Vincristine, Topotecan and Cyclophosphamide for Patients with Intermediate-Risk Rhabdomyosarcoma

**Principal Investigator:** COL Kelly J. Faucette, MC

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|-------------------------------|-----------------------|
| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
|-------------------------------|-----------------------|

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:intermediate-risk rhabdomyosarcoma, VAC, topotecan, pediatric cancer

**Start Date:**

2/22/2000

**Est. Completion Date:**

Feb 06

**Periodic Review:**

12/18/2001

**Study Objective:** (1) To compare the early response rates (i.e., CR/PR), failure-free survival (FFS) and survival of patients with intermediate risk rhabdomyosarcoma treated with surgery + RT and Vincristine, Actinomycin-D and cyclophosphamide (VAC) or the same alternating with a new combination which substitutes topotecan for actinomycin D (VAC/VTC/VAC), (2) To compare the acute and late effects of these two treatment regimens, (3) To determine the rate of second-look surgery in selected patients with bulk residual tumor at diagnosis (i.e., Clinical Group III) and the proportion of these that render the patient "tumor free" or with microscopic tumor only, (4) To determine the rate of local failure in selected patients with bulk residual tumors at diagnosis (i.e., Clinical Group III) who, following second-look resection, have response-adjusted radiotherapy dose reduction (36 Gy if in complete response or 41.4 Gy for microscopic residual disease), (5) To determine if preoperative radiotherapy followed by second-look surgery for selected patients with bulk residual disease (i.e., Clinical Group III) who respond poorly to induction chemotherapy is feasible, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by a positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

**Technical Approach:** This study will introduce topotecan to the standard therapy for intermediate risk rhabdomyosarcoma, surgery + RT and Vincristine, Actinomycin D, and Cyclophosphamide (VAC). This randomized study will compare two chemotherapy regimens, VAC versus VAC alternating with Vincristine/Topotecan/Cyclophosphamide (VTC) cycles.

**Progress:** No subjects enrolled in this study at MAMC in FY02. One subject was accepted as a transfer from Seattle, Washington during FY01. Subject enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/049                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> D9902: A Group Wide Protocol for Collecting and Banking Pediatric Cancer Research Specimens. An Intergroup Rhabdomyosarcoma Study Group Protocol  |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                       |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                                       |
| <b>Keywords:</b> Cancer:rhabdomyosarcoma, tumor tissue, pediatric cancer research specimens   |  |                                       |
| <b>Start Date:</b><br>2/22/2000   | <b>Est. Completion Date:</b><br>Feb 10 | <b>Periodic Review:</b><br>12/18/2001 |
| <b>Study Objective:</b> (1) To facilitate the collection of human tissue and other biologic specimens (blood, bone marrow) from Intergroup Rhabdomyosarcoma Study Group (IRSG) investigators, (2) To provide a repository for long-term storage of tissue and other biologic specimens (blood, bone marrow) collected by IRSG investigators (referred to as the Bank), and (3) To make available, through the IRSG/Cooperative Human Tissue Network, these materials for approved projects by laboratory-based investigators. |  |                                       |
| <b>Technical Approach:</b> At the time of initial diagnosis of rhabdomyosarcoma or undifferentiated sarcoma (or at re-excision of the primary tumor, if it occurs prior to the start of chemotherapy), surgical tissue, bone marrow and blood that are no longer needed for diagnosis will be prepared and shipped to the Pediatric Cooperative Human Tissue Network (CHTN) for Banking and Distribution.   |  |                                       |
| <b>Progress:</b> One subject enrolled in FY 02 and one in FY 01 for a total of two subjects enrolled in this study at MAMC. Subject enrollment continues.   |  |                                       |

### Detail Summary Sheet

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|------------------------|-----------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/072 | <b>Status:</b> Terminated |
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**Title:** POG 7837: Evaluation of Systemic Therapy for Children with Lymphoblastic Lymphoma Including T-Cell Disease

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** LTC Stephen R. Palmer, MC; MAJ Robert G. Irwin, MC

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**Keywords:** Cancer:pediatric lymphoblastic lymphoma, t-cell disease, cyclophosphamide, Ara-C, hydrocortisone, l-asparaginase, BCNU, hydroxyurea, methotrexate, prednisone, vincristine, 6-thioguanine

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**Start Date:**  
5/22/1998

**Est. Completion Date:**  
Pend

**Periodic Review:**  
5/14/2002

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**Study Objective:** (1) To evaluate a program of intensified CNS therapy for patients with lymphoblastic lymphoma, including T-cell leukemia, treated with the Pediatric Oncology Group's most successful systemic therapy schedule for these patients. This protocol will serve as the control arm for a randomized study, (2) to assess the toxicity and rate of complications encountered by patients receiving POG modified LSA2L2 Therapy in comparison with patient who received therapy using POG 7839 Treatment Arm 1 or POG 7615, (3) to assess the value of cranial radiation therapy plus 3-drug intrathecal chemotherapy in treating occult T-cell leukemia of the central nervous system, using the rate of CNS relapse and the rate of CNS complications for comparison with responses achieved using POG 7837 Treatment Arm 1 and POG 7615 therapy in pediatric patients with T-cell acute lymphocytic leukemia, (4) to assess the therapeutic effectiveness as measured by disease-free survival of POG Modified LSA2L2 Therapy (POG 7837 Treatment Arm 2) compared with responses achieved with POG 7837 Treatment Arm 1 and POG 7615 in pediatric patients with lymphoblastic lymphoma and T-cell leukemia, (5) to provide uniform therapy for patients with lymphoblastic lymphoma, including T-cell leukemia, so as to examine the response of immunologically defined subgroups of T-cell patients to this therapy, and in those patients for who marker studies have been obtained, to correlate response with histopathology and serologic markers, (6) to provide a common protocol for the treatment of patients with widespread T-cell malignancy, offering the opportunity for comparison of response rates among patients who have differing extent of disease.

**Technical Approach:** This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 1 patient being followed who was consented on an IRB approved 7837 study at Tripler AMC. Follow-up information on this patient will need to be sent to the POG Statistical Office per protocol requirements.

**Progress:** This protocol was terminated when consent to further contact was withdrawn by the one subject being followed.



## Detail Summary Sheet

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|--|--------------------------------------|-------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 98/073                | <b>Status:</b> Ongoing              |
| <b>Title:</b> POG 8602: Evaluation of Treatment Regimens in Acute Lymphoid Leukemia of Childhood (ALinC #14)   |                                      |                                     |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |                                      |                                     |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                |                                     |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC   |                                      |                                     |
| <b>Keywords:</b> Cancer:Pediatric acute lymphoid leukemia, calcium leucovorin, Ara-C, hydrocortisone, L-asparaginase, Erwinia L-asparaginase, mercaptopurine, methotrexate, prednisone, vincristine, Elliot's B  |                                      |                                     |
| <b>Start Date:</b><br>5/22/1998  | <b>Est. Completion Date:</b><br>Pend | <b>Periodic Review:</b><br>4/9/2002 |
| <b>Study Objective:</b> (1) To test the concept that intensive asparaginase (ASP) therapy, designed to maintain low asparagine levels for the first six months of maintenance will improve the outcome for patients with standard risk acute lymphocytic leukemia (ALL) when added to pulses of intermediate dose methotrexate (IDM), as compared to intensification with IDM alone, (2) to study the effectiveness in standard risk patients of intensification with a potentially synergistic or additive drug pair, i.e., IDM plus arabinosyl cytosine (AraC), as compared to that of intensification with IDM pulses alone, (3) to determine if administering a pulse of IDM + AraC at three week intervals (early intensification) during the first 4 months of complete remission in children with ALL is superior to administering the same number of IDM + AraC pulses at 12 week intervals (late intensification) during the first two years of complete remission in children with ALL with either "lower" or "higher" risk of relapse, (4) to obtain further information on the immediate and delayed toxicity of the continuation chemotherapy program that incorporates these combinations of methotrexate (MTX) and AraC or MTX and ASP in moderately high doses, (5) to continue to characterize the biological features of acute lymphatic leukemia of childhood, and their independence and interaction (with therapy and each other) as prognostic factors for attaining and maintaining remission, (a) To assess the effectiveness of these regimens for the early pre-B (non-T, non-B, non-pre-B) and pre-B immunophenotypes of All, respectively, (b) To investigate the hypothesis that ploidy and/or the presence of structural chromosome abnormalities predicts prognosis, (6) to learn whether outcome is related to individual patient differences in methotrexate (MTX) availability as measured by sequential determinations of red blood cell (RBC) MTX and folate levels. |                                      |                                     |
| <b>Technical Approach:</b> This study has closed to further patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 2 patients being followed who were consented on IRB approved 8602 studies in other POG institutions. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.   |                                      |                                     |
| <b>Progress:</b> Protocol closed to patient accrual. Three patients had been accepted in transfer from other POG institutions. One patient has been lost to follow-up and two continued to be followed during FY02.  |                                      |                                     |

### Detail Summary Sheet

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|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/076 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

**Title:** POG 8615: A Phase III Study of Large Cell Lymphomas in Children and Adolescents: A Comparison of Two Treatment Regimens - ACOP+ versus APO

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:lymphoma, pediatric cancer, ACOP, APO

**Start Date:**

5/22/1998

**Est. Completion Date:**

Indef

**Periodic Review:**

4/10/2002

**Study Objective:** (1) To determine the influence of alkylating agent (cyclophosphamide) therapy in advanced-stage large cell lymphomas in children and adolescents, by comparing in a randomized prospective study the efficacy and toxicity of a modified ACOP+ versus a modified APO regimen, (2) to reduce the adverse effects of treatments by elimination of involved field and cranial radiation in the treatment of large cell lymphomas, (3) to evaluate the adequacy of one year of total therapy for advanced large cell Non-Hodgkin's lymphoma (NHL), (4) to study clinical pathologic patterns and biologic characteristics of large cell lymphomas in children and adolescents, (5) to assess the feasibility of the total dose of Adriamycin of 300 mg/M2 on the APO arm (post closure of randomization).

**Technical Approach:** This study has closed to further patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 1 patient being followed who was consented on an IRB approved 8615 study at Stanford. Follow-up data on this patient will be forwarded to the POG Statistical Office per protocol requirements.

**Progress:** Protocol closed to enrollment, 8 Dec 92. One patient enrolled and continued to be followed during FY02.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 93/141                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 8650: Intergroup National Wilms' Tumor Study - 4  |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                      |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC |  |                                      |
| <b>Keywords:</b> Cancer;pediatric, Wilms'   |  |                                      |
| <b>Start Date:</b><br>6/9/1993  | <b>Est. Completion Date:</b><br>Oct 97 | <b>Periodic Review:</b><br>5/14/2002 |

**Study Objective:** To compare (1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D, (2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy, (3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy, and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

**Technical Approach:** All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

**Progress:** This protocol was closed to patient accrual 1 Sep 94. One patient enrolled at MAMC in FY93 and continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/074 | <b>Status:</b> Ongoing |
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**Title:** POG 8823/34: Recombinant Alpha-Interferon in Childhood Chronic Myelogenous Leukemia

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:Pediatric myelogenous leukemia, a-Interferon

**Start Date:**

5/22/1998

**Est. Completion Date:**

Pend

**Periodic Review:**

4/9/2002

**Study Objective:** (1) To determine toxicity, response rate and duration of response to therapy with recombinant alpha interferon for newly diagnosed “adult” chronic myelogenous leukemia (ACML) in chronic phase, and for “juvenile” chronic myelogenous leukemia (JCML) occurring within the first two decades. (2) to obtain prospective clinical, laboratory, and genetic data on cases of ACML and JCML treated with recombinant alpha interferon.

**Technical Approach:** This study closed to patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 3 patients being followed who were consented on IRB approved 8823 studies at Walter Reed Army Medical Center. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.

**Progress:** The protocol closed to patient accrual, 5 Jan 94; however, three patients continued to be followed during FY 02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 98/075                | <b>Status:</b> Ongoing              |
| <b>Title:</b> POG 9005: ALinC #15 - Dose Intensification of Methotrexate and 6-Mercaptopurine for ALL in Childhood - A Randomized Phase III Study   |                                      |                                     |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |                                      |                                     |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                |                                     |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC  |                                      |                                     |
| <b>Keywords:</b> Cancer:ALL, calcium leucovorin, Ara-C, hydrocortisone, L-asparaginase, Erwinia L-asparaginase, 6-mercaptopurine, methotrexate, prednisone, vincristine, pediatric cancer |                                      |                                     |
| <b>Start Date:</b><br>5/22/1998   | <b>Est. Completion Date:</b><br>Pend | <b>Periodic Review:</b><br>4/9/2002 |

**Study Objective:** (1) To determine, in a randomized trial, whether intensification with intermediate-dose methotrexate (ID MTX), and intravenous 6-mercaptopurine (IV 6-MP) is superior or inferior to repeated low-dose, oral methotrexate (LD MTX) and IV 6-MP for prevention of relapse in children with ALL in first remission and at lower risk for relapse, (2) To compare, in a randomized trial, intensification with ID MTX alone versus ID MTX and IV 6-MP for prevention of relapse in children with lower risk ALL in first remission, (3) To determine if RBC MTX/folate levels can be correlated with event free survival.

**Technical Approach:** This study closed to patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan has 6 patients being followed who were consented on IRB approved 9005 studies in other POG institutions. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.

**Progress:** This protocol closed to patient accrual, 1 Sep 94. There were a total of six patients enrolled at MAMC. One patient died in FY97 and five patients continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 95/018 | <b>Status:</b> Ongoing |
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**Title:** POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC

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**Keywords:** Cancer:medulloblastoma, cisplatin, VP-16, radiation, pediatric cancer

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| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
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11/18/1994

Nov 94

10/21/2002

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**Study Objective:** (1)To compare the 2-year event-free survival (EFS) of children with newly-diagnosed high-risk medulloblastoma who are treated with cisplatin and VP-16 pre-irradiation vs post-irradiation, (2) To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, (3) To determine whether achievement of a measurable tumor response (PR and CR) to pre-irradiation cisplatin/VP-16 has prognostic significance for children with high-risk medulloblastoma, compared with failure to achieve a measurable response (SD or PD), (4) To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, and (5) To determine if c-myc amplification in medulloblastoma is associated with an adverse prognosis.

**Technical Approach:** Studies in children and adults have demonstrated the ability to deliver pre-radiotherapy chemotherapy for patients with newly-diagnosed brain tumors without increasing neurotoxicity in association with the subsequent radiotherapy. This approach creates a phase II "window" allowing evaluation of response in these patients who are previously untreated except for surgery. The theoretical anti-neoplastic advantage of this approach is the potentially enhanced efficacy of the radiotherapy when given to "chemically debulked" patients. Half of the children diagnosed with medulloblastoma are now being successfully treated and are surviving for prolonged periods. Until recently, the survival of this group of patients was limited so that long-term effects of therapy were not a concern. As survival increases, one would expect to observe an increase in frequency of certain treatment-related toxicities. There are now a variety of long-term effects which need to be considered in this cohort of patients. Specific evaluations will be made on all patients entered onto this study, so that treatment-related problems may be detected in their early stages and intervention taken. This approach should ultimately improve the quality of life for children diagnosed and treated for brain tumors.

**Progress:** This protocol was closed to accrual 26 Mar 96. One patient enrolled in this study at MAMC (FY95) and continued to be followed during FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 95/056                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study   |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC  |  |                                      |
| <b>Keywords:</b> leukemia:pediatric, Cancer:leukemia:lymphoblastic, cytosine arabinoside, leucovorin calcium, hydrocortisone, 6-Mercaptopurine, methotrexate, E. coli asparaginase, Erwinia asparaginase, prednisone, vincritine   |  |                                      |
| <b>Start Date:</b><br>12/16/1994   | <b>Est. Completion Date:</b><br>Dec 99 | <b>Periodic Review:</b><br>12/2/2002 |
| <b>Study Objective:</b> (1) To confirm the outstanding results in patients with lesser risk not-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (AlinC 14, Arm A), (2) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.  |  |                                      |
| <b>Technical Approach:</b> Patients on this study will be treated with a 3-drug induction regimen (vincristine, prednisone, and L-asparaginase) to bring about remission (a state of no apparent disease) in four weeks. This will be followed by a consolidation phase including (6) six courses of intravenous (into vein) intermediate-dose methotrexate (each will require hospital stay) at 3-week intervals. After week 5, daily 6-mercaptopurine will be given by mouth until the end of planned treatment. Methotrexate will be given intramuscularly (into muscle) weekly. Periodic “pulses”(infrequent administration) of vincristine and prednisone will be given throughout the first two years of therapy. Additionally, triple intrathecal (into spinal fluid) therapy (TIT) consisting of methotrexate, hydrocortisone, cytosine arabinoside will be given at the start of treatment and periodically through the first two years of therapy to prevent the spread of leukemia to the central nervous system (CNS). The vitamin Leucovorin will be given to prevent methotrexate toxicity. After week 25, during the continuation phase, all medications will be on an outpatient basis. The total duration of therapy is planned to be 2 1/2 years from initial diagnosis. If tests at that time indicate no evidence of leukemia, then all medications will be stopped and you (your child) will be followed closely to be sure that there is no evidence of return of the disease. |  |                                      |
| <b>Progress:</b> This study closed to patient accrual 15 Nov 99. One patient enrolled in this study at MAMC in FY96 and another patient was accepted in as a transfer. Both continued to be followed during FY02.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/033 | <b>Status:</b> Ongoing |
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**Title:** POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; COL Bruce A. Cook, MC; COL Stephen R. Stephenson, MC; LTC Stephen R. Palmer, MC

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**Keywords:** Cancer:non-Hodgkin's, cyclophosphamide, adriamycin, prednisone, methotrexate, 6-mercaptopurine, ARA-C, hydrocortisone, pediatric cancer

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**Start Date:**

11/5/1993

**Est. Completion Date:**

Jun 96

**Periodic Review:**

10/21/2002

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**Study Objective:** (1) To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites, and (2) To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

**Technical Approach:** After staging, subjects that qualify will receive Vincristine 1.5 mg/M2 (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/M2/day in 3 divided doses x 28 days, Adriamycin 40 mg/M2/day IV days 1 & 22, and Cyclophosphamide 750 mg/M2/day IV days 1 & 22. Fluid intake is to be > 3000 ml/M2 on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries.

On day 43, or when blood counts recover, the patient will receive Adriamycin 40 mg/M2 IV, Cyclophosphamide 750 mg/M2 IV, Vincristine 1.5 mg/M2 (max 2 mg) IV, and Prednisone 50 mg/M2 in 3 divided doses x 5 days. On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

**Progress:** This protocol closed to patient accrual 2 Jul 99. Two patients enrolled in this study at MAMC FY97 and continued to be followed during FY02.



## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   |  |  | <b>Number:</b> 95/168                  |  |  | <b>Status:</b> Ongoing               |  |  |
| <b>Title:</b> POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study   |  |  |  |  |  |                                      |  |  |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |  |  |  |  |                                      |  |  |
| <b>Department:</b> Pediatrics  |  |  |  |  |  | <b>Facility:</b> MAMC                |  |  |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC   |  |  |  |  |  |                                      |  |  |
| <b>Keywords:</b> Cancer:Leukemia, ACML, inteferon, hydroxyurea, Ara-C, pediatric cancer  |  |  |  |  |  |                                      |  |  |
| <b>Start Date:</b><br>7/21/1995  |  |  | <b>Est. Completion Date:</b><br>Jul 99 |  |  | <b>Periodic Review:</b><br>5/14/2002 |  |  |
| <b>Study Objective:</b> (1) To assess the toxicity of the combination of Hydroxyurea (HU) and Ara-C combined sequentially with interferon-alpha 2b (IFN) in children with adult type chronic myelogenous leukemia (ACML), and (2) To determine the frequency and duration of hematologic and cytogenetic response, and the length of time needed to achieve response during two years of such treatment.   |  |  |  |  |  |                                      |  |  |
| <b>Technical Approach:</b> Therapy will be divided into 2 induction phases and a consolidation phase. Induction 1: Therapy will begin with two, or possibly three, weekly courses of hydroxyurea and Ara-C. Each course will consist of treatment given on three consecutive days as follows: after consuming clear fluids only for breakfast, hydroxyurea will be taken by mouth. Two hours later, Ara-C will be administered intravenously over 15 minutes. This will be repeated on the second and third day of each course. Subjects will receive at least two courses, beginning days 1 and 8. If blood counts are still above certain values on day 15, a third course will be given. Induction 2: Once blood counts have adequately recovered from the above chemotherapy, IFN treatment will begin. Subjects will receive IFN given as a subcutaneous injection daily for 14 days. Consolidation: IFN will then be continued at this dosage every Monday, Wednesday and Friday. IFN therapy will be interrupted for at least one week, approximately every 6 weeks, for a threeday course of hydroxyurea/Ara-C. This six-week cycle (IFN three times weekly for five weeks followed by a course of hydroxyurea/Ara-C), will be repeated for a total treatment time of approximately two years, assuming a good response to treatment. Most therapy will be administered at home (IFN) or in the outpatient clinic (hydroxyurea/Ara-C), with the exception being the first course of hydroxyurea/Ara-C and the first few days of IFN therapy, for which hospitalization is recommended. Every effort will be made to continue treatment for at least 90 days. All patients who have signs of progressive (worsening) disease within the first 90 days will be evaluated for possible discontinuation of this therapy. All other patients will continue on treatment for a total of 24 months. For those patients continuing on therapy past 90 days, the treatment will be discontinued (prior to 24 months) if there are signs of progressive disease at any time; if there is no evidence of any improvement by six months or if side effects develop which cannot be tolerated even with reduction in the drug dosages. Therapy may also be stopped at any time if a suitable marrow donor has been found and the physician decides that bone marrow transplantation would be in the patient's best interest. If the patient is still on therapy and responding well after 24 months, then the physician may offer to continue therapy with IFN alone. This will be offered as further therapy, but it will not be part of this study. It is not known how many years interferon may be safely given. The dosage schedule described above is to be considered a guideline. It is very possible that modification will need to be made depending on the side effects encountered. Routine blood tests will be done during the first four to six weeks of therapy (the "induction" phase), and then every one to two weeks while on therapy. A bone marrow aspirate and biopsy will be done prior to start of induction therapy, then twice more at about three month intervals, and then every six months thereafter unless removed from the study because of no response, progressive disease (increased severity), or bone marrow transplantation. A Chromosomal analysis will be completed on each bone marrow aspirate to find out if the Philadelphia chromosome is present. Each bone marrow aspirate will be followed by an ultrasound study of the spleen in order to determine the size of the spleen. |  |  |  |  |  |                                      |  |  |
| <b>Progress:</b> This protocol closed to patient accrual, 27 Jan 99. One patient enrolled in this study at MAMC in FY95, and was taken off study Jul 97 to pursue bone marrow transplant. This patient continued to be followed during FY02.   |  |  |  |  |  |                                      |  |  |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/092 | <b>Status:</b> Ongoing |
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**Title:** POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma

**Principal Investigator:** COL Kelly J. Faucette, MC

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| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

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**Keywords:** Cancer:sarcoma, doxorubicin, cisplatin, methotrexate, Ifosfamide, MTP-PE, pediatric cancer

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**Start Date:**  
4/1/1994

**Est. Completion Date:**  
Jun 99

**Periodic Review:**  
4/9/2002

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**Study Objective:** (1) To improve the survival of patients with osteogenic sarcoma, (2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma, (3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide, (4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery, (5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs, (6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma, (7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** This protocol was closed to patient accrual 25 Nov 97. Two patients entered in this study at MAMC in FY96. One patient chose to discontinue treatment early. The other patient has completed therapy. Both patients continued to be followed during FY02.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 95/087                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies  |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                      |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC |  |                                      |
| <b>Keywords:</b> Cancer:all types, HIV, Interferon, pediatric cancer  |  |                                      |
| <b>Start Date:</b><br>3/17/1995   | <b>Est. Completion Date:</b><br>Jun 99 | <b>Periodic Review:</b><br>2/20/2002 |

**Study Objective:** (1) To estimate the complete response rate for HIV related malignancies treated with interferon (aIFN), and (2) The secondary objectives are to estimate the one year disease free survival and to evaluate the toxicity of aIFN alone or in combination with anti-retroviral therapy.

**Technical Approach:** This study will require all patients to be enrolled in POG 9182 and compliance with all specimen submission requirements of that protocol. The study will minimize additional tissue, CSF or blood sampling except as required for monitoring for toxicity and tumor response. This study will take advantage of the demonstrated antitumor and antiviral activity of aIFN alone or in combination with other antiretroviral agents to treat HIV positive children with refractory or newly diagnosed malignancies. As the duration of response is one of the goals of this study, responders will continue on therapy indefinitely. Patients on this study will be treated using a interferon by subcutaneous injection every day for 14 days; then if your child's/adolescent's evaluation allows further treatment he/she will receive a interferon three times a week. This treatment will need to be monitored by a treating physician and blood tests will be performed in order to insure that the treatment is well tolerated and that the dose is appropriate. For that purpose 10cc of blood will be taken once a week. The physician and/or staff will be checking closely to see if any of these side effects are occurring. Routine physical exams, laboratory tests and tests such as biopsy or bone marrow aspiration may be necessary to monitor the effect of the treatment. Side effects usually disappear after the treatment is stopped. In the meantime, the doctor may prescribe medication to keep these side effects under control.

**Progress:** No patients enrolled in this study at MAMC in FY02. Patient enrollment continues.

### Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 95/058 **Status:** Ongoing

**Title:** POG 9400: ALinC 16 Classification (C) Protocol

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:leukemia:pediatric, laboratory classification

**Start Date:**

12/16/1994

**Est. Completion Date:**

Dec 99

**Periodic Review:**

12/2/2002

**Study Objective:** (1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission, (2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis, (3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t ( 9; 2 2 ) or t ( 1; 19 ) chromosomal abnormalities. (optional), (4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia, (5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional), (6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional), (7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL, and (8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

**Technical Approach:** A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

**Progress:** Ten patients are being followed by MAMC on this study. Six were enrolled at MAMC, three were transferred in from other facilities and four transferred out from MAMC. All ten patients are having follow-up data gathered by MAMC and furnished to the COG office.

## Detail Summary Sheet

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|--|--|--|-----------------------|--------------------------------------|--|
| <b>Date:</b> 30 Sep 02   |  | <b>Number:</b> 95/059                  |                       | <b>Status:</b> Ongoing               |  |
| <b>Title:</b> POG 9405: ALinC #16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)   |  |  |                       |                                      |  |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |  |                       |                                      |  |
| <b>Department:</b> Pediatrics  |  |  | <b>Facility:</b> MAMC |                                      |  |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC  |  |  |                       |                                      |  |
| <b>Keywords:</b> Cancer: leukemia pediatric, lymphoblastic leukemia, Calcium leucovorin, cytosine arabinoside, E. coli L-asparaginase, Erwinia L-asparaginase, hydrocortisone, 6-mercaptopurine, methotrexate, prednisone, vincristine   |  |  |                       |                                      |  |
| <b>Start Date:</b><br>12/16/1994   |  | <b>Est. Completion Date:</b><br>Dec 99 |                       | <b>Periodic Review:</b><br>12/2/2002 |  |
| <b>Study Objective:</b> (1) To determine in a randomized trial, the efficacy of a higher (2.5 gms/mt) versus standard (1 gm/m2) dose methotrexate (MTX) infusion during consolidation. The major endpoint will be eventfree survival among those achieving a complete remission. Secondary comparisons will include sitespecific events and adverse drug reactions, (2) To determine in a randomized comparison, the efficacy of delivering oral 6-MP on a once versus twice daily schedule during continuation, (3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405 and 9406, and (4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.   |  |  |                       |                                      |  |
| <b>Technical Approach:</b> In this research study, the subject will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as Prednisone, given orally (by mouth) for 28 days; Vincristine, given by a quick intravenous infusion (IV push) on days 1, 8, 15, and 22; L-asparaginase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, Cytarabine Arabinoside (Ara-C), and hydrocortisone will be administered intrathecally (injected into the spinal fluid) at various intervals throughout both the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. After Induction the subject will be randomized (assigned by chance, such as flipping a coin), to a specific regimen to include either standard or high dose IV Methotrexate and receiving oral 6MP once or twice daily. During the period of consolidation (weeks 5-28), the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP). The Methotrexate will be given at a standard or higher dose. In the first week, methotrexate will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. This 2 week treatment will be repeated for a total of 12 cycles. During the period of continuation (weeks 20-130), 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once each week. Patients randomized onto regimens B & D will receive 6MP orally twice daily. The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fail to achieve a complete remission during the induction phase of the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies. These studies will help the doctor to better understand this form of cancer and how treatment can be improved in the future. Chemotherapy given intrathecally into the spinal fluid may cause pain at infusion site, pain in the back, legs or head, fever, headache, vomiting; rarely stiff neck, convulsions, paralysis. Bone marrow aspiration may cause bruising and soreness over the bone from which the marrow sample is taken. |  |  |                       |                                      |  |
| <b>Progress:</b> This protocol closed to patient accrual, 26 Dec 95, due to excessive neurotoxicity. Two patients enrolled at MAMC. One patient enrolled in FY95 was taken off study but continues to be followed and the other who was enrolled in FY96 was transferred to another military treatment facility.   |  |  |                       |                                      |  |

## Detail Summary Sheet

**Date:** 30 Sep 02 **Number:** 95/060 **Status:** Ongoing

**Title:** POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC

**Keywords:** Cancer:leukemia pediatric, calcium leucovorin, ARA-C, E. coli asparaginase, Erwinia asparaginase, PEG asparaginase, hydrocortisone, Daunomycin, 6-mercaptopurine, methotrexate, prednisone, vincristine, VM-26

**Start Date:**  
12/16/1994

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
12/2/2002

**Study Objective:** (1) To determine the efficacy of a 2.5 gm/m<sup>2</sup> dose versus 1 gm/m<sup>2</sup> does intravenous methotrexate infusions during intensified continuation therapy. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events and adverse drug reactions, (2) To determine whether intensified continuation therapy delivering pulses of Ara-C (3 gm/m<sup>2</sup> x 4 doses) with asparaginase rescue is superior to standard intensified continuation with pulses of VM-26/Ara-C. The major endpoint will be event-free survival among those acheiving a complete remission.

**Technical Approach:** Children will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as prednisone, given orally for 28 days; vincristine, given by a quick intravenous infusion on days 1, 8, 15, and 22; L-asparaginase, injected IM on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, cytosine, arabinoside (Ara-C), and hyrocortisone will be administered intrathecally at various intervals throughout the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. Daunomycin will be given on days 8, 15, and 22 intravenously. After the previous treatment, subjects will be randomized to a specific regimen to include either standard or high does Methotrexate or low or high dose Ara-C. During the period known as consolidation, the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP) during weeks 5-6, 10-11, 15-16, 25-26, and 30-31. In the first week of each of these periods, methotrexate (either the standard or the intensified higher dose) will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle on day 1 and 6-MP daily by mouth for 7 days. At weeks 7, 17, and 27 the subject will receive Ara-C as a continuous infusion for 72 hours (higher dose) or injected under the skin (lower dose). VM-26 will be given as a 45-minute IV infusion before the start of Ara-C and on day 2 with standard dose Ara-C. If the subjectreceive intensified Ara-C, the subjectwill also receive the drugs PEG and G-CSF. PEG is a drug that may lessen the toxic effects of Ara-C, and G-CSF is used to increase the blood count to decrease the risk of infection. At weeks 12, 22, and 32, Ara-C will be infused over 72 hours as described above. Daunomycin (DNR) will be given as a 30-minute infusion before the start and at the end of the Ara-C. In addition to DNR/Ara-C, vincristine is given IV on days 1 and 8, prednisone by mouth on days 1 and 7, and PEG-L-asparaginase IM on day 1. During the period known as continuation, weeks 35-130, standard dose 6-MP will be given orally each day, and methotrexate injected into a muscle once a week. The total time of planned therapy is 130 weeks (2-1/2 years). The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study.

**Progress:** This study closed to patient enrollment 15 Nov 99. A total of 2 patients were enrolled in this study at MAMC, with no patient enrollment during FY02. Two patients received study treatment. One patient enrolled in the study treatment suffered an acute left frontal lobe hemmorrhage during induction therapy and was removed from the study. The second patient completed therapy and is still being followed.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 95/089                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML   |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC  |  |                                      |
| <b>Keywords:</b> Cancer:AML, ARA-C, Cyclosporine, multidrug resistance, pediatric cancer   |  |                                      |
| <b>Start Date:</b><br>3/17/1995  | <b>Est. Completion Date:</b><br>Jan 01 | <b>Periodic Review:</b><br>2/20/2002 |
| <b>Study Objective:</b> (1) To determine the effect of high dose vs. standard dose Ara-C induction on CR (clinical remission) and EFS (event free survival) in Childhood AML, (2) To compare EFS in Childhood AML after 3 cycles of consolidation with or without the MDR (multidrug resistance) modulator CSA (cyclosporine A), (3) To compare the EFS between patients genetically randomized between allogeneic BMT and chemotherapy, (4) To evaluate the impact of EFS of various clinical and laboratory factors such as cytogenetics and MDR expression, and (5) To confirm the superior response of Down syndrome patients utilizing standard induction and non-CSA containing consolidation, and identify specific biologic and pharmacokinetic characteristics in these patients.   |  |                                      |
| <b>Technical Approach:</b> Phase III evaluation of standard vs. high dose Ara-C induction followed by the randomized use of Cyclosporine A as an MDR (multidrug resistant) reversal agent, compared to allogeneic BMT, in childhood AML. Patients will be randomized (assigned by chance, such as flipping a coin) at the time of diagnosis to receive either standard doses or high doses of ARA-C during the initial course of therapy. The chances of receiving any of the therapies is approximately equal. Later in the course of therapy, patients (according to how they were previously randomized) will or will NOT receive the drug Cyclosporine A in combination with the chemotherapy agents, Mitoxantrone and Etoposide. Patients with Down syndrome will not be randomized, but will receive the standard therapy. Earlier studies have shown the three year event-free survival rate for Down syndrome children significantly superior to children without Down syndrome using standard therapy. Also, for this reason Down syndrome patients will not receive Cyclosporine A. If a sibling who is matched for bone marrow transplantation, will receive bone marrow transplantation, which has been shown to be a more effective treatment in controlling AML compared to chemotherapy, providing that consent from the sibling donor can be obtained. If not a sibling donor, studies have shown chemotherapy is superior to matched unrelated donor BMT. However, should the patient choose to pursue an unrelated matched BMT instead of continuing with consolidation chemotherapy, the subject may discontinue the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may also be used for research studies. |  |                                      |
| <b>Progress:</b> This study closed to patient accrual, 15 Aug 99. Two patients enrolled in this study at MAMC. One patient died and the other patient continued to be followed during FY02.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 97/054 | <b>Status:</b> Ongoing |
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**Title:** POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

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**Keywords:** Cancer:Hodgkin's, Zinecard, Irradiation, pediatric cancer

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**Start Date:**

2/21/1997

**Est. Completion Date:**

Jul 03

**Periodic Review:**

1/22/2002

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**Study Objective:** (1) To tailor chemotherapy courses based on the patients' initial response to therapy, (2) To examine the activity of variable courses of doxorubicin, bleomycin, vincristine, and etoposide (DBVE) and low-dose involved field irradiation, (3) To monitor safety and feasibility of the response-dependent approach, and morbidity, immediate and long term toxicities of the above regimen, (4) To evaluate if limited therapy is adequate for patients with early response, (5) To examine if addition of Zinecard can reduce pulmonary toxicity while not significantly reducing response rate or event-free survival, and (6) To determine if the frequency and magnitude of myocardial injury during therapy, as measured by an elevation of cardiac Troponin-T in the serum, is reduced by the addition of Zinecard.

**Technical Approach:** Registered study patients will be randomized to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 2 courses of the four drug combination etoposide, vincristine, bleomycin and doxorubicin at 28 day intervals. Patients will be restaged after receiving these two chemotherapy courses. Those showing remission will go on to radiation therapy, while those showing residual disease will receive 2 more courses of the four drug combination and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis.

**Progress:** This protocol closed to patient accrual, 19 Sep 00. Two patients enrolled in this study at MAMC have completed therapy and continued to be followed during FY02.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 96/097                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study  |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC   |  |                                      |
| <b>Keywords:</b> Cancer:Wilms, chemotherapy, radiation therapy, biology study, pediatric cancer  |  |                                      |
| <b>Start Date:</b><br>4/19/1996  | <b>Est. Completion Date:</b><br>Jul 02 | <b>Periodic Review:</b><br>4/23/2002 |
| <b>Study Objective:</b> (1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood, (2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis, (5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor, (6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide, (7) to improve survival of patients with malignant rhabdoid tumor of the kidney, (8) to study biology and pathology of patients who present with bilateral Wilms tumor, (9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines, and (10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine. |  |                                      |
| <b>Technical Approach:</b> This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages 1-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.  |  |                                      |
| <b>Progress:</b> The study was closed to accrual on 31 May 02. One patient enrolled in FY96 in this study at MAMC and then was transferred to Portsmouth Naval Hospital. One patient was accepted in transfer from Tripler AMC and continues to be followed. One patient was consented for this study in FY01; however, tumor tissue studies determined the patient was not eligible for study participation. One patient was diagnosed at MAMC on 1 Dec 01 and is still being followed.   |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/090 | <b>Status:</b> Ongoing |
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**Title:** POG 9442: National Wilms Tumor Late Effects Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:Wilm's tumor, frequency, fertility rates, congenital defects, gene disorders, second malignancy, congestive heart failure, pediatric cancer

**Start Date:**

7/17/1998

**Est. Completion Date:**

Jul 03

**Periodic Review:**

5/14/2002

**Study Objective:** To determine (1) the frequency of Wilms tumor and other cancers in family members of Wilms tumor patients in order to estimate the recurrence risk in siblings and offspring; test the plausibility of specific genetic modes of inheritance in homogeneous subgroups; and identify familial cancer syndromes (if any) that may involve Wilms tumor, (2) To determine fertility rates of Wilms tumor patients and rates of perinatal mortality, low birth-weight and adverse pregnancy outcomes in relation to the type and amount of cancer treatment received in childhood, (3) To estimate the rates of selected congenital defects and of specified single gene disorders (sentinel phenotypes) in the offspring of Wilms tumor patients, (4) to estimate the rates of second malignancy neoplasms in relation to the dosage of radiation therapy and the use of specific chemotherapeutic agents (actinomycin D, doxorubicin, cytoxan and etoposide) received in childhood, (5) to compare the incidence rate of congestive heart failure among Wilms tumor survivors in relation to the dose of radiation therapy received to abdomen and/or lungs and to the use of specific chemotherapeutic agents.

**Technical Approach:** The large number of Wilms tumor survivors ascertained by the NWTS during its first twenty years of operation constitutes an ideal cohort for the study of familial risk and late effects of treatment. Four protocol studies have been conducted; treatment protocols and results for the first three studies have been published. A large fraction of the total national U.S. incidence of Wilms tumor has been registered on these studies, probably as much as 70% of an estimated 450-500 cases occurring nationally since 1980. Over 2,500 children who were followed on NWTS treatment protocols have now survived 5 or more years since their original diagnosis. Many of those treated more than a decade ago have reached sexual maturity, so that their reproductive history and the status of their offspring may be evaluated by entry into this study.

**Progress:** No patients enrolled in this study at MAMC in FY02. Subject enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 96/035                  | <b>Status:</b> Ongoing                |
| <b>Title:</b> POG 9490: Topotecan Followed by Multimodal, Multiagent Therapy for Children and Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study   |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                       |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC   |  |                                       |
| <b>Keywords:</b> Cancer:rhabdomyosarcoma, Topotecan, pediatric cancer  |  |                                       |
| <b>Start Date:</b><br>11/17/1995   | <b>Est. Completion Date:</b><br>Jun 97 | <b>Periodic Review:</b><br>10/21/2002 |
| <b>Study Objective:</b> (1) To evaluate the toxicity of the topoisomerase I inhibitor, topotecan, when given alone at a maximum tolerated dose by bolus injection daily X 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease, (2) To estimate the response rate (complete or partial) of such patients to topotecan, and (3) To evaluate the toxicity of a new chemotherapy combination comprising topotecan, cyclophosphamide, and vincristine (VTC) given in alternating cycles with vincristine, actinomycin D, and cyclophosphamide (VAC) to patients who have achieved an objective response partial response (PR) or complete response (CR) to topotecan. |  |                                       |
| <b>Technical Approach:</b> Patients with rhabdomyosarcoma, clinical stage IV disease will receive Topotecan upfront at 2.0 mg/M2/day X 5 IV. Following evaluation, patients with partial response or complete response will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 in conjunction with vincristine and cyclophosphamide. Continuation therapy begin following evaluation at week 25 with VAC/VTC for patients showing PR and CR.   |  |                                       |
| <b>Progress:</b> This protocol closed to patient accrual, 1 Nov 96. One patient enrolled in this study at MAMC FY96 and continued to be followed in FY02   |  |                                       |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 96/120 | <b>Status:</b> Ongoing |
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**Title:** POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

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**Keywords:** Cancer:leukemia, lymphoblastic, methotrexate, 6-mercaptopurine, pediatric cancer

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**Start Date:**

5/17/1996

**Est. Completion Date:**

Jul 03

**Periodic Review:**

4/9/2002

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**Study Objective:** (1) To determine in a randomized trial whether the addition of 6 months of delayed intensification with divided dose oral methotrexate (ddMTX) improves event-free survival (EFS) of children with standard risk acute lymphoblastic leukemia, (2) to determine in a randomized trial the effect on EFS of delivering oral 6-mercaptopurine (6-MP) on a divided (twice daily) vs once a day schedule, during delayed intensification and continuation, (3) to study how laboratory data from POG 9400 correlates with outcome by pooling studies 9201, 9405, 9605, and 9406, (4) to assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy, and (5) to describe the occurrence of elevated transaminases and correlation of these with outcome.

**Technical Approach:** This treatment protocol involves 130 weeks of chemotherapy beginning with standard induction therapy of generally 4 (but up to 6) weeks of chemotherapy consisting of vincristine, prednisone, and L-asparaginase plus triple intrathecal therapy of combined methotrexate, hydrocortisone and Ara-C. Post induction, the treatment is divided into consolidation, intensification, and maintenance phases of therapy. Registration on study occurs post induction therapy at which time patients are randomized to receive 1 of 4 regimens which vary beginning in the intensification phase of therapy.

**Progress:** This protocol closed to patient accrual, 15 Nov 99. There are now five (5) patients being followed at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/045                  | <b>Status:</b> Ongoing                |
| <b>Title:</b> POG 9631: A Phase II Feasibility Study of Oral Etoposide Given Concurrently with Radiotherapy Followed with Dose Intensive Adjuvant Chemotherapy for Children with Newly-Diagnosed High Stage Medulloblastoma  |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                       |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC   |  |                                       |
| <b>Keywords:</b> Cancer:medulloblastoma, etoposide, vincristine, cisplatin, cyclophosphamide, G-CSF, radiotherapy, pediatric cancer  |  |                                       |
| <b>Start Date:</b><br>2/23/1999  | <b>Est. Completion Date:</b><br>Feb 05 | <b>Periodic Review:</b><br>12/18/2001 |
| <b>Study Objective:</b> (1) To estimate the response rate and toxicity of children with newly diagnosed high-stage medulloblastoma who are treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (2) To compare the response rate and toxicity of these patients to historical control patients registered on POG study # 9031 TRT 2 (RT alone followed by adjuvant chemotherapy), (3) To estimate the 2-year event-free survival and overall survival of patients treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (4) To compare the 2-year event-free survival and overall survival of these patients to historical control patients registered on POG study # 9031, and (5) To evaluate the toxicity of dose intensive chemotherapy following craniospinal irradiation using oral etoposide, cisplatin, cyclophosphamide and vincristine. |  |                                       |
| <b>Technical Approach:</b> The goal of this study is to maximize response to initial therapy using oral etoposide concurrently with radiotherapy in children with newly diagnosed high stage medulloblastoma. Adjuvant therapy will continue after radiation using dose intensive chemotherapy.  |  |                                       |
| <b>Progress:</b> No subjects enrolled in this study in FY02 at MAMC. Subject enrollment continues.   |  |                                       |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/066 | <b>Status:</b> Ongoing |
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**Title:** POG 9720: Idarubicin and Cladribine in Recurrent and Refractory Acute Myeloid Leukemia: A Pediatric Oncology Group Phase II Study

**Principal Investigator:** COL Kelly J. Faucette, MC

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| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Keywords:** Cancer:pediatric, myeloid leukemia, idarubicin, cladribine

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| <b>Start Date:</b><br>3/20/1998 | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b><br>2/20/2002 |
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**Study Objective:** (1) To determine the CR rate of the combination of Idarubicin (IDA) and Cladribine (CDA) in patients with recurrent AML, (2) To determine the CR rate of the combination of IDA and CDA in patients with primary refractory AML, (3) To determine the CR rate of the combination of IDA and CDA in patients with recurrent or primary refractory secondary AML and myelodysplastic syndromes (not related to Down's Syndrome), (4) To determine the toxicities of the combination of IDA and CDA, and (5) To define the pharmacokinetics of CDA administered as a 2 hour infusion.

**Technical Approach:** Eligible patients will be stratified and receive a five day treatment consisting of IV Idarubicin daily for 3 days and IV Cladribine, 2 hours daily for 5 days. Twenty-four hours after completion of chemotherapy, patients will begin daily subcutaneous injections of G-CSF until blood counts stabilize. A bone marrow aspirate will be done at 3 weeks to assess response. A second course may be given. If patients have progressive disease they will be taken off study.

**Progress:** No patients enrolled in this study in at MAMC in FY02. Subject enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/053                 | <b>Status:</b> Completed              |
| <b>Title:</b> POG 9836: Treatment of Children with Diffuse Intrinsic Brain Stem Glioma with Standard Dose Irradiation and Vincristine Plus Oral VP-16   |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                       |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC; LTC William B. Reece, MC; LTC Stephen M. Yoest, MC   |  |                                       |
| <b>Keywords:</b> Cancer:Brain Stem Glioma, oncology, Vincristine, VP-16, radiation therapy, pediatric cancer  |  |                                       |
| <b>Start Date:</b><br>1/23/2001   | <b>Est. Completion Date:</b><br>Jan 04 | <b>Periodic Review:</b><br>12/18/2001 |
| <b>Study Objective:</b> (1) To evaluate the efficacy of oral VP-16, Vincristine, and conventional dose radiation therapy on one year survival in children with newly diagnosed brain stem glioma and (2) monitor the toxicity of this therapy in children with newly diagnosed brain stem glioma.   |  |                                       |
| <b>Technical Approach:</b> The prognosis for children with diffuse intrinsic brain stem glioma is disappointing. The usual treatment of children with diffuse, intrinsic brain stem glioma is radiation therapy to the involved area. Recent reports have shown very encouraging results using oral Etoposide for children with recurrent brain stem glioma. The purpose of this study is to determine the effectiveness of vincristine in combination with VP-16 and irradiation in patients with newly-diagnosed brain stem glioma, and also to determine the type of side effects that occur when vincristine, VP-16 and radiation therapy are given together. |  |                                       |
| <b>Progress:</b> C.O.G. reported this study closed to enrollment, effective 14 Dec 01. No patients enrolled in this study at MAMC   |  |                                       |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/032 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** POG 9900: ALinC 17 Classification (C) Protocol, A POG Non-therapeutic Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:children's leukemia, lymphoma, biological classification, pediatric cancer

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jan 05

**Periodic Review:**  
1/22/2002

**Study Objective:** (1) To provide the clinical and laboratory data necessary for placing each patient with ALL onto proper therapeutic trial, and (2) to provide an administrative base to capture classification data for correlative studies in ALL treatment protocols and series of historical protocols.

**Technical Approach:** At the time of diagnostic evaluation which includes bone marrow aspiration and/or biopsy, 20 ml of bone marrow and 25 ml of peripheral blood will be collected and processed for local laboratory studies and submission to the following POG reference laboratories: 1. Johns Hopkins University for Immunophenotyping. 2. University of New Mexico (UNM) for DNA Index, FISH, Molecular testing, Cell banking. 3. Medical College of Wisconsin for Glucocorticoid receptors. 4. University of Texas Southwestern Medical Center for Homocysteine Children's Hospital of Michigan for Drug sensitivity profiles. 5. MUSC - Children's Hospital for Drug sensitivity profiles. UCSD Medical Center for Tumor suppressor gene studies. The data captured on this protocol will be used in the therapeutic trials, in cross era analysis, and in international collaborations to further define the prognostic importance of biologic features in ALL.

**Progress:** Four subjects enrolled in FY 02, and four subjects were enrolled in previous years, for a total of eight subjects enrolled in this study at MAMC. Subject enrollment continues.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/077                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9904: ALinC 17 Protocol for Patients with Newly Diagnosed Low Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC  |  |                                      |
| <b>Keywords:</b> Cancer:ALinC 17, childrens leukemia, Low-risk ALL, pediatric cancer   |  |                                      |
| <b>Start Date:</b><br>5/12/2000  | <b>Est. Completion Date:</b><br>May 04 | <b>Periodic Review:</b><br>4/23/2002 |

**Study Objective:** (1) In conjunction with POG 9905, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity. (2) to determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL, (3) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (4) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This protocol will randomize between the 4-hour and 24 hour methotrexate infusion and for patients with TEL/AML1 gene, between standard and delayed intensification. Data from POG 9904 and 9905 will be pooled for statistical analysis of efficacy and toxicity. This study will determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). Induction will include three or four drugs (dependent on initial risk classification POG 9900).

**Progress:** No subjects enrolled in FY02, two subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 200/076      **Status:** Ongoing

**Title:** POG 9905: ALinC 17 Protocol for Patients with Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:ALinC 17, childrens leukemia, Standard-risk ALL, pediatric cancer

**Start Date:**

5/12/2000

**Est. Completion Date:**

May 04

**Periodic Review:**

4/23/2002

**Study Objective:** (1) To determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL. This objective will also be assessed as part of POG protocol 9904; (2) In conjunction with POG 9904, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity; (3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): (a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; (b) Marrow morphology on day 8, and; (c) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples on day 29 and after consolidation; (4) Using a case control design, quantitate MRD with flow cytometry and molecular techniques, to determine whether late relapse correlates with a given level of MRD in marrow samples obtained and banked at the completion of therapy. To analyze samples obtained at relapse to ascertain whether markers of MRD remain constant i.e., if a relapse not "predicted" by high levels of MRD in remission samples, is it because of a change in the identified markers.

**Technical Approach:** This study will utilize a 2 x 2 factorial design to answer two randomized questions. The standard arm will recapitulate regimen A of the current POG protocol for standard risk patients. Induction will include three or four drugs (dependent on initial risk classification POG 9900) and consolidation will include 24-hour MTX infusions, at one gram per square meter, given every three weeks for a total of six doses. The two randomizations will assign patients to receive therapy with or without the delayed intensification and receive the IV MTX as a 2 gm/m<sup>2</sup> infusion over four hours versus a one gram per m<sup>2</sup> infusion over 24 hours. Intensive continuation will include 4 cycles of therapy with each 12 week cycle including 6 courses of divided dose oral MTX, nightly 6-MP, a dose of intrathecal MTX and a pulse of vincristine and dexamethasone. Standard continuation therapy includes weekly MTX, daily 6-MP and vincristine/dexamethasone pulses every 16 weeks. Dexamethasone replaced prednisone in the 9705 pilot study, and will be utilized here because of better CNS penetration and data suggesting that its use enhance event-free survival. The current POG study for standard risk patients includes a randomization to single versus twice daily dosing of oral 6-MP, based on the concept that duration of exposure is critical to anti-metabolite efficacy. This study includes only the traditional single nightly dose. Should the results of the open trial suggest an advantage to the use of divided dose 6-MP, this protocol will be amended.

**Progress:** Two subjects enrolled in this study in FY02, two enrolled in FY01 and one in FY00 for a total of five subjects enrolled at MAMC. Subject enrollment continues.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/075                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG 9906: ALinC 17 Protocol for Patients with Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL), Evaluation of the Augmented BFM Regimen, a POG Phase III Study |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC   |  |                                      |
| <b>Department:</b> Pediatrics  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC  |  |                                      |
| <b>Keywords:</b> Cancer:ALinC 17, childrens leukemia, High-risk ALL, pediatric cancer  |  |                                      |
| <b>Start Date:</b><br>5/12/2000  | <b>Est. Completion Date:</b><br>May 04 | <b>Periodic Review:</b><br>4/23/2002 |

**Study Objective:** (1) To determine for patients at high risk for treatment failure if the augmented Berlin-Frankfurt-Munster (A-BFM) therapy is superior to ALinC 14/15 therapy, on the basis of historical controls; (2) To determine if minimal residual disease at the end of induction is predictive of an inferior prognosis; (3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; b) Marrow morphology on days 8, and 29; 4) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples and at the end of induction and therapy, (5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (6) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis, and (7) To give Pediatric Oncology Group (POG) investigators experience with BFM-type regimens as these will likely play a major role in Children's Oncology Group (COG) protocols of the future.

**Technical Approach:** The regimen as defined by POG 9906 will represent a modified version of CCG augmented BFM for patients at high risk for treatment failure as defined by ALinC 17 clinical and biological criteria. Routine whole brain irradiation will not be used. Instead we will rely on intrathecal chemotherapy, except for those with established CNS disease at diagnosis. However, the augmented BFM results remain unsatisfactory for subsets of patients in the following categories: Philadelphia chromosome positive, hypodiploid (<45) modal chromosome number, and M-3 marrow at day 29. Both CCG and POG analyses concur that these groups, comprising approximately 3-4% of newly diagnosed patients with A.L.L., have an EFS <45%. These cases, henceforth classified as Very High Risk, will be entered on a separate combined POG/CCG (COG) trial evaluating new chemotherapy and marrow transplant strategies. Risk group assignment will be determined otherwise by the method of using age, WBC, CNS status, DNA index, and molecular and cytogenetic criteria as established for POG ALinC 17 classification protocol.

**Progress:** One subject enrolled in FY02 and one in FY01, for a total of two subjects enrolled in this study at MAMC. Subject enrollment continues.

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/010 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** POG 9917: A Pilot Study of Dose Intensification of Methotrexate in Patients with Advanced Stage (III/IV) Small Non-cleaved Cell Non-Hodgkin's Lymphoma and B-cell ALL

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:Acute Lymphoblastic Lymphoma,Methotrexate, pediatric cancer

**Start Date:**  
10/24/2000

**Est. Completion Date:**  
Oct 10

**Periodic Review:**  
10/21/2002

**Study Objective:** (1) To determine if increasing the Methotrexate dose from 1 gm/m<sup>2</sup> to 5 gm/m<sup>2</sup> in combination with standard treatment as per the POG 9317 protocol is feasible in a group-wide setting, and to assess the toxicity of this intensified therapy, (2) to assess the feasibility of treating patients with CNS disease at diagnosis with VP16/Ifosfamide plus the intensified chemotherapy, in order to confirm the superior survival of this group of patients when treated in this fashion, (3) to prospectively assess toxicities and late effects of such intensive chemotherapy on the central nervous system, cardiac function, and fertility, (4) to informally estimate the costs of hospitalization for the treatment of therapy-related side effects and (5) to evaluate the biology of Burkitt and Burkitt-like NHL and B-ALL with respect to the REAL classification, and to assess the feasibility of obtaining tissue for important biology studies in a group-wide setting.

**Technical Approach:** This study will be opened to newly diagnosed patients with Stage III and IV NHL and B-ALL with or without CNS disease. The patient's diagnosis will determine the order and frequency of the treatment. Treatment for Stage III and IV NHL and B-ALL without CNS disease will consist of Induction and Consolidation Therapy (Stage III patients will repeat only cycle A of Consolidation therapy and Stage IV patients will repeat an entire cycle, A & B, of Consolidation therapy). Patients with CNS disease will receive Induction, Intensification and Consolidation therapy also repeating cycles A & B of Consolidation therapy. Chemotherapy drugs utilized in this study are Doxorubicin, Leucovorin Calcium, Cytosine Arabinoside, Cyclophosphamide, Mesna, Methotrexate, G-CSF, Vincristine, Dexamethasone, Ifosfamide, Etoposide.

**Progress:** This study closed to patient enrollment, 7 Oct 02, as C.O.G. reported accrual goals for the study had been met. No patients enrolled in this study at MAMC.

## Detail Summary Sheet

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|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/051                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> POG A2971: Treatment of Children with Down Syndrome and Acute Myeloid Leukemia, Myelodysplastic Syndrome, or Transient Myeloproliferative Disorder, a Phase III Group-Wide Study  |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                       |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                                       |
| <b>Keywords:</b> Cancer:leukemia, myelodysplastic syndrome, pediatric cancer  |  |                                       |
| <b>Start Date:</b><br>1/23/2001   | <b>Est. Completion Date:</b><br>Jan 07 | <b>Periodic Review:</b><br>12/18/2001 |
| <p><b>Study Objective:</b> (1). To evaluate the efficacy (as compared to DS children enrolled on CCG 2891) of reduced dose chemotherapy for DS patients diagnosed with AML or MDS: (1.1) to maintain or improve the current remission rate (94%) in this population of children with low risk (for relapse) disease, and (1.2) to maintain or improve the current disease-free survival rate (88%), (1.3) to reduce acute morbidity &amp; mortality in this high risk (for toxicity) population and (1.4) to determine whether there is a reduction of sequelae in long term survivors. (2). To define our understanding of the natural history of TMD by: (2.1) Establishing a CCG database for patients with TMD, (2.2) Establishing the use of uniform treatment guidelines for TMD, (2.3) Establishing the incidence of subsequent leukemia, and (2.4) Delineating predictive risk factors for subsequent leukemia. (3). To facilitate biologic investigations of leukemia in DS patients through banking of biologic specimens. (4). To facilitate epidemiologic investigations of leukemia in DS patients.</p> <p><b>Technical Approach:</b> This study builds upon CCG-2891 and utilizes a reduced variation of DCTER induction, standard timing, to reduce toxicity and maintain or increase efficacy. The added benefits of etoposide and dexamethasone in the DCTER regimen during induction in the DS population is uncertain. The experience with daunomycin, cytarabine (Ara-C), and 6-thioguanine is extensive and is an effective combination during induction. The use of DCTER's (minus the VP16 &amp; steroid) method of administration (continuous infusion) has several advantages in this population, including reduction of long-term cardiac toxicity risk. It is better tolerated than pulse administration, and it is a similar method to the control group (CCG-2891DS patients). As Capizzi II was very well tolerated in this group in CCG-2891, and its efficacy in maintaining DFS has been well established, this therapy will be maintained and will be identical to that given in CCG 2961. This will avoid the possibility of a reduction in DFS at the end of this study without knowing whether the reduction of therapy during induction or during intensification was the cause. TMD: Patients with TMD will be identified utilizing a common diagnostic criteria, treated with a uniform protocol, and then monitored consistently and prospectively. This methodology will permit a truer description of the natural history of this unusual disease. The eligibility criteria utilized within this study will be broad so as to better define this entity. A subgroup will be identified utilizing diagnostic criteria set forth in the current Pediatric Oncology Group observational study of TMD to permit future collaborative efforts. It will as well, by virtue of its longitudinal design permit biologic studies to investigate and elucidate the mechanisms by which this proliferative disease naturally comes under control. Utilizing the nested case-control methodology we will be able to compare, within the cohort of patients with TMD, those who develop AML versus those who do not, and then identify both clinical and biologic prognostic factors. These two groups will also allow examination to determine what biologic mechanisms are present which suppress or fail to suppress eventual neoplastic development.</p> <p><b>Progress:</b> No current patients are enrolled in this program at MAMC, we are leaving open for additional enrollment.</p> |  |                                       |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/100 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** POG A3961: Treatment for Infants and Children with Intermediate Risk Neuroblastoma: A Pediatric Oncology Group/Children's Cancer Group Phase III Intergroup Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:intermediate risk neuroblastoma, pediatric cancer

**Start Date:**

6/27/2000

**Est. Completion Date:**

Jun 07

**Periodic Review:**

5/14/2002

**Study Objective:** (1) To determine that Intermediate Risk Neuroblastoma with favorable biology will have a >90% event free survival (EFS) and survival (S) with a short course of chemotherapy (4 cycles) over 84 days without primary radiation therapy, (2) To determine that Intermediate Risk Neuroblastoma with unfavorable biology will have a >90% (EFS) with a longer course of chemotherapy (8 cycles) over 168 days without primary radiation therapy, and (3) To determine the acute and long term morbidity/toxicities associated with treating Intermediate Risk Neuroblastoma with surgery and chemotherapy.

**Technical Approach:** This study is an intergroup Phase III prospective nonrandomized trial to evaluate reduced therapy for intermediate risk neuroblastoma based on clinical and selected biologic, prognostic variables in order to maintain event free survival and survival, and minimize both acute and long-term morbidity in this group of patients. Either prior to or after study entry, patients will undergo an operation to remove as much of the primary tumor and involved lymph nodes as can be safely accomplished with minimum morbidity. Intermediate risk patients with favorable biology will receive 4 cycles of chemotherapy. Second surgery will be done for all patients not in complete remission following recovery from the 4th cycle of chemotherapy. Intermediate risk patients with unfavorable biology will continue with an additional 4 cycles of chemotherapy for a total of 8 cycles. At the conclusion of 8 cycles, the patient shall undergo second surgery. Radiotherapy will be administered to the site of viable residual disease after completion of 8 weeks of chemotherapy and second look surgery for selected intermediate risk INSS Stage 3 or 4 neuroblastoma patients with unfavorable biology.

**Progress:** No patients enrolled in this study at MAMC during FY02. Subject enrollment continues.

### Detail Summary Sheet

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|---|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/138                 | <b>Status:</b> Ongoing              |
| <b>Title:</b> POG A9952: Chemotherapy for Progressive Low Grade Astrocytoma in Children Less Than Ten Years Old |  |                                     |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                     |
| <b>Department:</b> Pediatrics   |  | <b>Facility:</b> MAMC               |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                                     |
| <b>Keywords:</b> Cancer:progressive low grade astrocytoma, pediatric cancer, Pediatric Oncology Group,          |  |                                     |
| <b>Start Date:</b><br>9/26/2000   | <b>Est. Completion Date:</b><br>Sep 07 | <b>Periodic Review:</b><br>8/8/2002 |

**Study Objective:** To compare the event-free survival as a result of treatment with both carboplatin and vincristine (CV) or a combination of thioguanine, procarbazine, CCNU, and vincristine (TPCV).

**Technical Approach:** After as complete as possible surgical resection, without causing increased neurological deficits, a child will be followed without further intervention until signs of progression are observed. Children with progressive symptoms due to tumor and minimal surgery are also eligible without initial follow-up. Children with NF and definitive progression of optic pathway tumors can be entered without surgery. At registration children will be randomly assigned to either CV or TPCV chemotherapy. All children with NF will be non-randomly assigned to CV. All children will be followed until signs of definite tumor progression. The children will not be taken off chemotherapy for stable disease since this may be a desirable outcome.

**Progress:** No patients enrolled in this study at MAMC during FY02. Subject enrollment continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/052 | <b>Status:</b> Ongoing |
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**Title:** POG P9462: Randomized Treatment of Refractory Neuroblastoma with Topotecan Regimens, Following Deferoxamine (POG only) in an Investigational Window, A POG/CCG Phase II Intergroup Study

**Principal Investigator:** COL Kelly J. Faucette, MC

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| <b>Department:</b> Pediatrics | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC

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**Keywords:** Cancer:Refractory neuroblastoma, Topotecan, deferoxamine, pediatric cancer

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**Start Date:**

1/23/2001

**Est. Completion Date:**

Jan 04

**Periodic Review:**

12/18/2001

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**Study Objective:** Topotecan regimen: To compare Topotecan alone with the combination of topotecan + cyclophosphamide in terms of response rate, toxicity and time to disease progression. Deferoxamine (DFO) window (POG only):To determine the response rate to and toxicity of DFO and the relationship between serum DFO levels and the biological effects, toxicity and efficacy of DFO.

**Technical Approach:** This study hypothesizes that there are differences in efficacy among the two regimens utilizing topotecan that are under investigation currently; topotecan IV daily x 5, and topotecan plus cyclophosphamide IV daily x 5. Phase I and II studies have demonstrated that neuroblastoma is sensitive to the topotecan IV daily x 5 and the topotecan plus cyclophosphamide IV daily x 5 regimens. The efficacy of adding topotecan to an aggressive multidrug chemotherapy regimen to treat patients newly diagnosed with neuroblastoma will be tested in future phase III randomized studies. In this study of patients with recurrent neuroblastoma, a randomized trial will be conducted in order to determine which of these two topotecan regimens should be tested in the future phase III studies.

**Progress:** No patients currently enrolled at MAMC, protocol remains open for new enrollment.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 98/065                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> POG P9641: Primary Surgical Therapy for Biologically Defined Low-Risk Neuroblastoma; A Pediatric Oncology Group Children's Cancer Group, Phase III, Intergroup Study  |  |                                      |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                      |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC  |  |                                      |
| <b>Keywords:</b> Cancer:pediatric, neuroblastoma, surgery, carboplatin, etoposide, cyclophosphamide, doxorubicin  |  |                                      |
| <b>Start Date:</b><br>3/20/1998   | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b><br>2/20/2002 |
| <b>Study Objective:</b> (1) To determine if low risk INSS stage 2A/2B asymptomatic neuroblastoma patients treated with surgery alone will have a three year survival (S) rate of 95%, (2) To determine if low risk INSS stage 1 asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (3) To determine if low risk INSS stage 4S asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (4) To estimate the response and 3 year event-free survival (EFS) rates of symptomatic patients with chemotherapy, (5) To estimate the EFS and S rates in patients who relapse or progress after initial treatment with surgery alone, (6) To determine the acute and long-term morbidity/toxicities associated with treating low-risk neuroblastoma with surgery alone or with surgery and chemotherapy, (7) To further define and evaluate the prognostic importance of other biologic factors as determined on studies POG #9047 (or its successor), CCG #B973, and by International Neuroblastoma Risk Group criteria, (8) To collect resource utilization data regarding number of hospital days, the extent of transfusion support, and the use of diagnostic imaging, and to compare these with historical CCG study 3881 data. |  |                                      |
| <b>Technical Approach:</b> Patients in this study will be stratified by stage and extent of disease to either surgery alone or surgery with chemotherapy. Further studies done on patient's tumor specimens may change their classification to "intermediate" or "high" risk neuroblastoma, in which case they will be taken off study and more intensive chemotherapy will be administered.  |  |                                      |
| <b>Progress:</b> No subjects were enrolled during FY02. One patient enrolled in FY01 at MAMC and continues to be followed. Subject enrollment continues.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/127 | <b>Status:</b> Completed |
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**Title:** POG P9749: Pilot Intergroup Study of High-Dose Cisplatin, Etoposide and Bleomycin (HD-PEB) Combined with Amifostine in Children with High-Risk Malignant Germ Cell Tumors

**Principal Investigator:** COL Kelly J. Faucette, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Kenneth S. Azarow, MC; COL Jerome B. Myers, MC; COL Marc G. Cote, MC

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**Keywords:** Cancer:germ cell tumors, cisplatin, etoposide, bleomycin, amifostine, pediatric cancer

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**Start Date:**  
8/28/2001

**Est. Completion Date:**  
Jul 03

**Periodic Review:**

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**Study Objective:** Primary: (1) To evaluate the early efficacy and toxicity profile of administering high dose cisplatin, etoposide, and bleomycin (HD-PEB) in combination with amifostine to children with high-risk malignant germ cell tumors (GCT) and (2) whether the use of amifostine can reduce the hematologic and non-hematologic toxicities of HD-PEB in these patients when compared to similar patients treated on POG 9049/CCG 8881 with HD-PEB. Secondary: (3) To estimate the response rate of patients with high-risk malignant GCT to HD-PEB with amifostine, (4) to collect samples and facilitate studies which distinguish alpha-fetoproteins of liver and germ cell tumor origins, (5) to facilitate studies & sample collection of germ cell tumor cytogenetics, molecular genetics, and amplification of c-myc, (6) to facilitate studies & sample collection for studies of DNA repair mechanisms in germ cell tumors, (7) to derive tumor cell lines and xenografts of germ cell tumors for use in studies of biologic agents such as experimental chemotherapeutic agents and differentiation agents and (8) to establish a biologic samples bank for germ cell tumors to include frozen tumor, frozen normal tissue, patient blood and parental blood that will be used in future studies that will impact on the clinical care and prognosis of affected patients.

**Technical Approach:** Induction therapy will consist of four cycles of HD-PEB with amifostine administered at 21-day intervals. Patients > 12 months of age will be pre-treated with amifostine at a dose of 825 mg/m<sup>2</sup> /dose IV over 15 minutes beginning 30 minutes prior to cisplatin administration. After four cycles of HD-PEB, patients will have complete diagnostic imaging evaluation. Patients in clinical CR will electively stop therapy. Patients in clinical PR will have second-look surgery and if there is residual tumor will be eligible to receive two more cycles of HD-PEB. Patients in clinical CR after six cycles will electively stop therapy. Patients not in CR after six cycles will be off study.

**Progress:** C.O.G. reported this study closed to enrollment, effective 23 Apr 02, as accrual goals had been met. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

|   |  |                                       |
|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/050                 | <b>Status:</b> Completed              |
| <b>Title:</b> POG P9754: Protocol for Patients with Newly-Diagnosed Non-Metastatic Osteosarcoma, A POG/CCG Pilot Intergroup Study   |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                       |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                                       |
| <b>Keywords:</b> Cancer:non-metastatic osteosarcoma, Childrens Oncology Group   |  |                                       |
| <b>Start Date:</b><br>2/22/2000   | <b>Est. Completion Date:</b><br>Feb 06 | <b>Periodic Review:</b><br>12/18/2001 |
| <b>Study Objective:</b> (1) To sequentially perform three pilot studies of dose intensified therapy for osteosarcoma: a) doxorubicin dose intensification, b) doxorubicin dose intensification with ifosfamide, c) alkylator intensification. One of these therapies will be used in a randomized study whose objectives will be: (1.1.) To determine whether postoperative dose intensification can improve outcome for standard responders to preoperative chemo therapy, (1.2.) To determine whether the use of dexrazoxane (DXR) cardioprotection during a standard preoperative induction regimen affects histologic response, (2) To pilot a standard preoperative chemotherapy regime n administered with dexrazoxane (DXR) cardioprotection for all newly diagnosed patients with non-metastatic osteosarcoma, (2.1.) To test whether DXR can be safely used with doxorubicin in combination with cisplatin (pilot 1) or cisplatin/ifosfamide (pilots 2,3), (2.2.) To ascertain that the cytotoxicity as measured by tumor necrosis at definitive surgery is not compromised by the used o DXR compared to historic control, (3) To assess the feasibility of administering 600 mg/m2 of doxorubicin with DXR cardioprotection (pilot 1,2) or high dose ifosfamide the etoposide (pilot 3) to standard risk patients who are also being treated with methotrexate and cisplatin (and ifosfamide in pilots 2,3), (4) To evaluate the feasibility of obtaining tumor tissue for analysis of biologic factor in osteosarcoma in conjunction with P9851, and (5) To evaluate the feasibility of assessing musculoskeletal, cardiac, renal and gonadal status after the completion of therapy. |  |                                       |
| <b>Technical Approach:</b> Two courses of standard chemotherapy will be given prior to surgery, limiting intensification to the population at greatest risk. The cohort with a good response to therapy will continue with non-intensified chemotherapy. For the purposes of this study, good responders will have greater than or equal to 98% necrosis in the tumor specimen resected at definitive surgery. The companion biology protocol POG P9851 will accompany this study.  |  |                                       |
| <b>Progress:</b> C.O.G. reported this study closed to enrollment, effective 11 Feb 02. No patients enrolled in this study at MAMC.  |  |                                       |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/018 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** POG P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors: A COG Study

**Principal Investigator:** COL Kelly J. Faucette, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Keywords:** Cancer:Refractory solid tumors, Irinotecan, pediatric cancer

**Start Date:**

11/19/1999

**Est. Completion Date:**

Nov 04

**Periodic Review:**

10/22/2002

**Study Objective:** (1) To determine the efficacy of irinotecan in the treatment of children with refractory neuroblastoma, sarcomas of soft tissue or bone, other solid tumors, or brain tumors, (2) to further evaluate the toxicity of irinotecan when given daily for 5 days, repeated every 21 days, and (3) to further evaluate the pharmacokinetics/pharmacodynamics of irinotecan and its metabolites SN-38, SN 38G, and APC, using a limited sampling strategy.

**Technical Approach:** Irinotecan appears to be one of the most active topoisomerase I inhibitors that is clinically available and therefore deserves further evaluation in children with recurrent CNS or solid tumors. Although the optimal schedule for irinotecan is not yet known, antitumor activity has been observed on all schedules of administration. Pharmacokinetic studies, an integral component of this trial will be done to determine if there are correlates with PK parameters and toxicity or response.

**Progress:** One patient enrolled in this study in FY00 at MAMC, however, Peds Hem/Onc reported this patient's death, due to Influenza A, 26 Jun 01. An SAE report was filed stating the possibility that this death could have been a result of the study drug due to delayed neutropenia. There were no patients enrolled during FY02. Patient enrollment continues.

### Detail Summary Sheet

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|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/048                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies |  |                                       |
| <b>Principal Investigator:</b> COL Kelly J. Faucette, MC  |  |                                       |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC   |  |                                       |
| <b>Keywords:</b> Cancer:osteosarcoma, tumor tissue, biologic studies, pediatric cancer              |  |                                       |
| <b>Start Date:</b><br>2/22/2000   | <b>Est. Completion Date:</b><br>Feb 10 | <b>Periodic Review:</b><br>12/18/2001 |

**Study Objective:** (1) To increase our understanding of the basic biology of these tumors, with a distinct possibility that new therapeutic targets may be uncovered. Examples of this type are ErbB-2 and methotrexate resistance factors, (2) To develop a set of biologic prognostic indicators which can be measured at diagnosis and which will be predictive of response and outcome in osteosarcoma. These could then be used in subsequent treatment programs to determine therapy, avoiding excessive toxicity to good risk patients and reserving alternative, more intensive therapy for those at standard risk. Examples include loss of heterozygosity at Rb and MDR, (3) To determine the feasibility of various assays and to develop a reliable mechanism of distributing osteosarcoma samples to various intergroup investigators, with centralized reporting of laboratory results and adequate quality control.

**Technical Approach:** At the time of biopsy or surgery (definitive or recurrence), tumor tissue that is not needed for diagnosis will be processed and forwarded to the Cooperative Human Tissue Network (CHTN) for distribution. Specimens will include: tumor tissue (Formalin-fixed or formalin-fixed paraffin embedded block or 30 unstained slides; blood samples (heparinized (10 ml), serum (14 ml)). Assays being performed: MDR Immunohistochemistry (University of Rochester); MDR Functional Assays/MRP (Memorial Sloan-Kettering); Methotrexate Transport & Metab (Memorial Sloan-Kettering); Topoisomerase II (Yale University); Bcl-2/Bax (Yale University); Rb/p53 (Fels Institute); ErbB-2 (Memorial Sloan-Kettering); MDM2 (Memorial Sloan-Kettering); p16/p21 (Hospital for Sick Children); LOH at 3q,18q (Fels Institute); sis, gli, fos (Yale University); SV40 (University of Colorado); myc, RAS (Memorial Sloan-Kettering); metalloproteinase (Yale University); c-met/HGF (Yale University); IGF-I/IGF-IR (University of Maryland); Telomerase (St. Jude Children's); Ploidy (Dana Farber)

**Progress:** No patients enrolled in this study at MAMC in FY02. Subject enrollment continues.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/092 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Management of Diabetes Mellitus in Young Children: A Survey of Pediatric Endocrinologists

**Principal Investigator:** CPT Britney G. Frazier, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** COL Robert J. Newman, MC; MAJ Donald R. McClellan, MC

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**Keywords:** diabetes intensive management DCCT

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**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Sep 02

**Periodic Review:**

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**Study Objective:** To determine whether pediatric endocrinologists are using intensive diabetes management in children less than 13 years old.

**Technical Approach:** Surveys to be mailed to approximately 750 pediatric endocrinologists regarding their current management of children with type I diabetes mellitus. Descriptive analysis of the results will be used to determine current standard therapy of pre-adolescents with type I diabetes.

**Progress:** During FY 2002, survey was written and prepared for mailing. Background research continues. The surveys have not yet been mailed out to the endocrinologists. Zero responses in FY 02.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/126                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Ibuprofen Oral Provocation Challenge in Children with Asthma  |  |                                      |
| <b>Principal Investigator:</b> COL Donald R. Moffitt, MC  |  |                                      |
| <b>Department:</b> Pediatrics   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> COL Edward R. Carter, MC; CPT Mitchell Moffitt, MC; Gregory Redding, M.D.; Jason Debley, M.D. |  |                                      |
| <b>Keywords:</b> asthma, children, ibuprofen, bronchoconstriction   |  |                                      |
| <b>Start Date:</b><br>8/28/2001   | <b>Est. Completion Date:</b><br>Sep 02 | <b>Periodic Review:</b><br>7/16/2002 |

**Study Objective:** To estimate the prevalence of ibuprofen-induced bronchoconstriction in children with mild to moderate asthma and identify those clinical variables or characteristics that may correlate with ibuprofen-induced bronchoconstriction, to include age, sex, history of nasal polyps, history of sinusitis, history of eczema, history of allergic rhinitis, asthma medications, history of prior NSAID use, and asthma severity.

**Technical Approach:** This study will be performed jointly by investigators at the Pulmonary Division of Children's Hospital, Seattle and the Department of Pediatrics at Madigan Army Medical Center. The study is designed to determine the prevalence of ibuprofen-induced bronchospasm in children with mild or moderate asthma. Approximately 50 children with asthma, ages 6-18 years, will be enrolled at Madigan and another 150 at the Seattle Children's Hospital in this prospective, double-blind, placebo control, crossover study. The inclusion criteria are: a diagnosis of mild or persistent asthma, a baseline FEV1 > 70% of the predicted value, and the ability/willingness of the patient to swallow capsules; exclusion criteria are: not being able to swallow capsules, taking a leukotriene inhibitor for their asthma, and experiencing increased asthma signs/symptoms. Patient's asthma must be stable and well controlled. Children who have mild or moderate asthma, based on standard criteria, will be asked to fill out an asthma questionnaire and participate in two separate pulmonary function test sessions, each lasting approximately 4.5 hours. During these study sessions patients will perform baseline spirometry and then ingest by mouth either capsules containing 100mg of ibuprofen (10 mg/kg up to a maximum dose of 600 mg) or identically appearing placebo capsules. Patients will then perform spirometry at 0, 1, 2, and 4 hours post-ingestion of the capsules. Patients will return to the laboratory 2-7 days later for the second session. The order of administering placebo and ibuprofen will be randomized. Patients will be monitored and examined by a physician during all study time points. Precautions will be taken to ensure prompt and effective treatment of bronchospasm. Once patient's FEV1 decreases to < 80% of the baseline value, on that study day sessions will be stopped, and no further testing will be done. Primary outcome measure is the proportion of patients who meet the criteria for ibuprofen-induced bronchospasm. The criteria to be used to determine this is a decrease in FEV1 post-ibuprofen ingestion of / 20% from baseline without a decrease in FEV1 on the placebo study day.

**Progress:** Work on this protocol has not yet been initiated. COL Moffitt recently assumed the role of PI for this study following the retirement of the previous PI, COL Carter.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/102 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** The Relationship Between Urgent Care and Emergency Department Visits for Asthma and Air Quality in Tacoma-Pierce County

**Principal Investigator:** COL Donald R. Moffitt, MC

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**Department:** Pediatrics

**Facility:** MAMC

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**Associate Investigator(s):** COL Edward R. Carter, MC; Jane Koenig; Janet Primomo, Ph.D.

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**Keywords:** asthma air pollution emergency department urgent care

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**Start Date:**

8/27/2002

**Est. Completion Date:**

Dec 04

**Periodic Review:**

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**Study Objective:** 1. To identify risk factor, e.g. air pollution, which contributes to asthma exacerbations. 2. To examine the relationship between daily visits to urgent care and emergency departments and air quality indicators.

**Technical Approach:** In order to conduct this study we will collect daily air pollution data and daily counts of visits to urgent care centers and EDs for asthma during the years 2002-2004. Daily air pollution levels will be obtained from the Puget Sound Clean Air Agency and the Washington State Department of Ecology. The pollutants of interest are particulate matter (PM), sulfur dioxide, ozone and carbon monoxide. We will obtain the daily counts of asthma visits to urgent care centers and EDs from each of the participating medical treatment facilities. For each asthma visit identified we will record the patient's age and gender, the date of the visit, the ICD9 diagnoses and the zip code of the patient's residence. Then we will correlate volume of patient visits with concentrations of the various pollutants.

**Progress:** Work on this protocol has not yet been initiated. COL Moffitt recently assumed the role of PI for this study following the retirement of the previous PI, COL Carter.



### Detail Summary Sheet

|   |  |                         |
|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/134                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Establishment of a Primary Myocyte Cell Culture Line from Dystrophin-deficient (mdx) Mouse Embryonic Fibroblasts (Mus musculus) |  |                         |
| <b>Principal Investigator:</b> CPT Robert J. Organ, MC  |  |                         |
| <b>Department:</b> Pediatrics   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> Steven X. Skapek, MD  |  |                         |
| <b>Keywords:</b> cyclin D1, mdx mice, cell culture  |  |                         |
| <b>Start Date:</b><br>9/19/2001   | <b>Est. Completion Date:</b><br>Sep 04 | <b>Periodic Review:</b> |

**Study Objective:** Establish primary myocyte cell cultures from mdx mouse embryonic fibroblasts (MEFs) with the DNA construct pBABEpuroMyoD, and wild type mdx MEFs. ii. Demonstrate a dependent relationship in dystrophin- deficient myocytes between the activation of NF-kB, the aberrant expression of cyclin D1, and the presence of apoptosis.

**Technical Approach:** This study proposes establishing primary myocyte cell cultures from mdx and wild type Mouse Embryonic Fibroblasts (MEF). It has already been established that it is extremely difficult to obtain a pure population of mdx myoblasts in culture; others have demonstrated that cultures of mdx myoblasts from neonatal to adult mice don't grow properly<sup>51,52,53,54</sup>. To overcome this problem we propose establishing mdx mouse embryonic fibroblasts in culture, a procedure already well established (see attached methodology). 6 mice will be purchased; 3 mdx and 3 controls. The 2 females of each group will be impregnated, and then at the appropriate time the females will be euthanized and the embryos will be harvested for embryonic fibroblasts. We will then transduce these cells with a gene that will cause them to start differentiating into myoblasts. The transduction of the embryonic fibroblasts will produce a cell line of primary myoblasts from both the wild type mouse and the dystrophin-deficient (mdx) mouse.

**Progress:** Preliminary studies reveal that we have successfully transduced both mouse mdx and wild type embryonic fibroblasts into myocytes as planned. We have been able to successfully demonstrate the presence in both of these cell lines of myoD and myosin, 2 proteins only found in myocytes. In addition to refining our staining technique, remaining work on this protocol includes demonstrating the presence of dystrophin in the wild type cell cultures and the absence of dystrophin in the mdx mice to confirm our genotypes. We hope to accomplish this by Western blots.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/104      **Status:** Ongoing

**Title:** Newborn Infant Speech Perception

**Principal Investigator:** MAJ Randall C. Zernzach, MC, USAF

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** Lori A. Loan, Ph.D.; Christine Moon, PhD

**Keywords:** newborn infant, speech perception, language acquisition

**Start Date:**  
6/13/2001

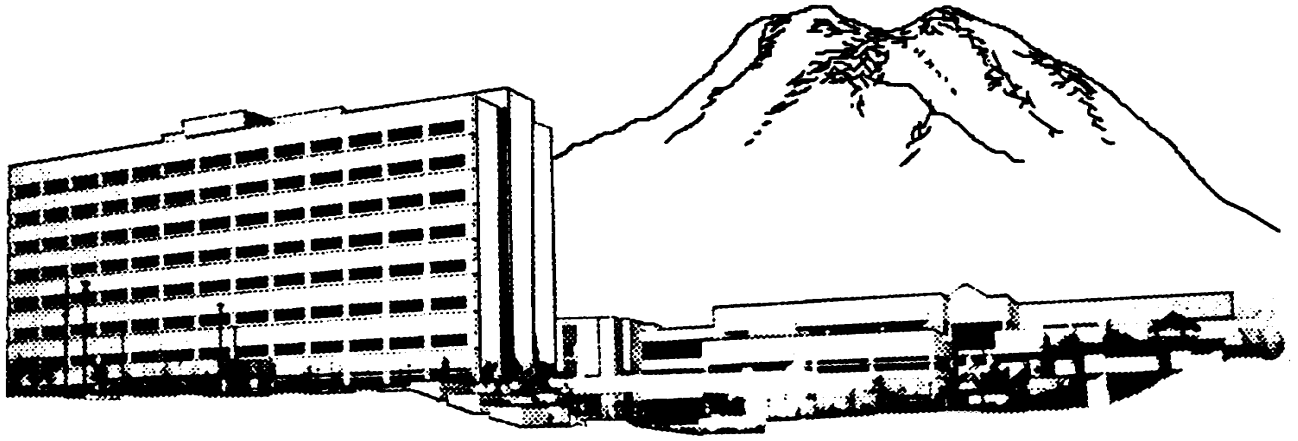
**Est. Completion Date:**  
May 03

**Periodic Review:**  
6/7/2002

**Study Objective:** Characterize the effect of experience on typically developing newborn infants' perception of speech and language.

**Technical Approach:** The current proposal for research is for a 2-year study of newborn infant discrimination of familiar and unfamiliar speech sounds. Three experiments will comprise the study. The first will test newborns' ability to discriminate mother's voice from a stranger voice when the speech samples are brief. The second experiment will examine whether infants respond preferentially to their mother's native language when the samples are brief. In the third experiment, infants will be tested for their ability to discriminate brief vowel sounds from among well- and poorly-formed exemplars in English. Each of the three experiments will require data from 80 participants for a total of 240 infants. Because the attrition rate for completion of the 10-minute session is likely to be about 35%, it is expected that approximately 360 infants will be recruited and that 120 will not complete the experiment. Prospective participants will be 1-5 days old and will be identified from hospital records. Eligibility will be based upon criteria that indicate typical, uncomplicated newborn development. Parents will be contacted in their hospital rooms by the experimenters who will present the study and obtain signed, informed consent. Infants will be transported to a quiet area near the newborn unit for a 20-minute session. A pacifier that is connected to a pressure transducer will be placed in the infant's mouth. If the pacifier is accepted, headphones will be placed over the infant's ears. After a 1-minute baseline period to measure sucking pressure, computer-controlled sounds at conversational levels of intensity will be presented for 9 minutes, contingent upon infant sucking pressure. Frequency of sucks during particular stimuli will be the dependent measure. Data analysis will be based upon a comparison of sucking frequency during different sounds. Results of the experiments will be presented at professional conferences and submitted as articles for publication in professional journals.

**Progress:** 86 subjects have been recruited during FY02. Results thus far have contributed to two abstracts sent out in Sep 02. Conclusions thus far: (1) within the range of women's normal speaking voices, pitch alone is not an important factor in neonatal preference for voices; (2) there is behavioral evidence that neonates can recognize their mother's voice with only a very brief (750ms) voice sample.



**Detail Summary Sheets**

**Preventive Medicine Service**

### Detail Summary Sheet

|   |  |                          |
|---|--|--------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/051                 | <b>Status:</b> Completed |
| <b>Title:</b> Health Care Burdens of Multiple Marker Maternal (MMM) Screening   |  |                          |
| <b>Principal Investigator:</b> MAJ Paul D. Benne, MD, MPH   |  |                          |
| <b>Department:</b> Preventive Medicine  |  | <b>Facility:</b> MAMC    |
| <b>Associate Investigator(s):</b> MAJ Andrew R Wiesen, MC   |  |                          |
| <b>Keywords:</b> multiple marker maternal screen, triple screen, triple marker, labeling, false positive, Down syndrome, open fetal defect, neural tube defect, Trisomy 18, Edward's syndrome |  |                          |
| <b>Start Date:</b><br>3/26/2002   | <b>Est. Completion Date:</b><br>Mar 02 | <b>Periodic Review:</b>  |

**Study Objective:** The objective of this study is to determine the outcome of multiple marker maternal (MMM) screening on maternal mental health and labeling of the resulting infant.

**Technical Approach:** Mental health morbidity amongst those exposed to MMM screening and those not exposed will be compared. Mental health morbidity will be evaluated by comparing usage rate of antidepressant and anxiolytic medication and mental health care visits. Furthermore, the role of labeling will be observed by comparing rates of infant health care usage in excess of well baby visits. Labeling would infer the treatment of false positives as if they are diseased (Gordis). Groups compared within the cohort will be stratified as to the result of screening (true and false positives and negatives). The number of subjects studied allowing this stratified analysis, using a prevalence of depression in the unexposed group of 10% (ACOG) and an anticipated relative risk of 1.5 is 6600 subjects. Pregnant women cared for at Puget Sound Regional Medical Treatment Facilities during 1996 - 2000 will be observed. Women excluded will be those with multiple gestation beyond twins or two or more of the following: diabetes, anti-convulsant therapy, prior birth of Down Syndrome, open fetal defect or trisomy 18. Birth defect registries and further data from Genzyme genetics, the manufacturer of the test used at MAMC, will be used to validate true positive and false negatives. Logistic regression will be used to find an adjusted odds ratio of mental health morbidity in this population.

**Progress:** This study was reported as completed, Jun 02; however an abstract of findings is not yet available.

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/090

**Status:** Completed

**Title:** Development of an ADS-based Syndromic Surveillance System Using Sexually Transmitted Diseases as a Prototypic Sentinel Condition

**Principal Investigator:** LTC James E. Cook, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** COL Jeffrey D. Gunzenhauser, MC; COL Kelly T. McKee, Jr., MC; CDR Randy Culpepper, MC (Navy); MAJ Andrew R. Wiesen, MC

**Keywords:** ambulatory data system, ADS, geographic information system, GIS, sexually transmitted diseases, surveillance

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
July 01

**Periodic Review:**  
5/3/2002

**Study Objective:** (1) To build an interface between the Ambulatory Data System (ADS) and a Geographic Information System (GIS) by linking these systems to extract information on outpatient Sexually Transmitted Diseases from 2 geographically distinct Army installations: Fort Bragg, NC, and Fort Lewis, WA, and (2) To verify ADS diagnoses reported through CEIS by linkage with laboratory data on tests performed to diagnose syphilis, gonorrhea, and chlamydia contained in CHCS at Madigan Army Medical Center.

### Technical Approach:

The study population is any Madigan beneficiary who had a lab test performed for an acute STD syndrome (syphilis, gonorrhea, or chlamydia), who had an ICD-9 diagnosis for an acute STD syndrome (same) recorded in CEIS via ADS, or both. The study period is 1 Jan 97 through 31 Dec 99. To ensure that lab tests or clinic visits occurring on the margins of the study period are identified and included, data will actually be collected for the period Dec 1996 through January 2000, but will eventually be truncated to delete information on any beneficiaries for whom BOTH the lab test and the clinic visit occurred outside of the study period. Beneficiaries for whom at least one of these events occurred within the study period will be included in the analysis.

Patients with ADS-based diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be identified in central CEIS data files by one of the research collaborators. Information extracted from CEIS will include FMP, SSN, date of birth, clinic visit location, date of clinic visit, and ICD-9 coded diagnosis. Patients with diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be extracted from the Madigan CHCS system by the principal investigator using the ad hoc query. Information extracted from CHCS will include FMP, SSN, gender, date of birth, address of beneficiary (street address, city, state, and ZIP code), date of lab test, lab test result, and MEPRS code of the clinic (medical resource center) at which the test was ordered.

These two data acquisition efforts will identify all persons with a positive laboratory diagnosis for an acute STD syndrome, a positive ICD-9 diagnosis for the same acute STD syndromes, or both. However, because the primary analytic technique of the study will be McNemar's 2x2 table, information will also be needed on beneficiaries who had both a negative lab test and an ADS-based ICD-9 diagnosis for a condition other than an acute STD syndrome. To complete this cell of the 2x2 table, patients at Madigan who had a negative test for syphilis (RPR/VDRL), gonorrhea (culture or GenProbe), or chlamydia (Chlamydiazyme or GenProbe) during the study period will be identified. Their SSNs and FMPs will be collected in a data set and sent to associate investigator to batch merge with CEIS to identify ICD-9 codes resulting from clinic visits during which these diagnostic tests were performed. The merging of these two data sources will in this way identify persons for whom both a CHCS-recorded test was performed and an ICD-9 code was entered in

ADS from the related clinic visit, both of which are NEGATIVE for a diagnosis of an acute STD. This approach is exhaustive in identifying all persons who fit these criteria during the study period.

The study method described will require that personally identifying information must be shared between investigators on the East Coast and at Madigan. Specifically, information on patients with positive diagnosis for acute STD syndromes will need to be sent from the CEIS extraction origin to the investigator at Madigan to validate whether or not a lab test was performed and what the result was. Similarly, personal identifiers on all Madigan patients for whom a diagnostic test for an acute STD syndrome is recorded in CHCS will need to be sent to the CEIS POC to ascertain whether an encounter was documented in ADS (CEIS) and whether a diagnosis of an acute STD syndrome was recorded.

To protect privacy, efforts will be made to safeguard data. Names of beneficiaries will not be abstracted from either source. Family Member Prefix (FMP) coupled with the sponsor Social Security Number (SSN) will serve as the means of record linkage. Once all data has been collected, data from the two sources (CEIS and CHCS) will be merged (by FMP and SSN). Dates of birth will be converted to ages. After merging and age conversion, FMPS, SSNs, and DOBs will be eliminated from the data set. Address information will be maintained, however, to allow for precise mapping of beneficiary residence. If the GIS program purchased for this study is unable to use specific street address information, this field will be deleted, and only city, state and zip code information will be maintained in the final data set used for analysis. Geographic information data usable in a GIS system (ArcView or comparable software) will be purchased or downloaded from the Internet. Clinical data will be merged into the GIS to plot frequencies of specific diagnoses by Zip Code, SMSA, or county of residence, as the GIS software will allow.

**Progress:** Work on this study was reported completed, May 02. The project had been intended to produce a software platform for syndromic surveillance as initiated by the original principal investigator, COL Gunzenhauser; however, funding for the project has been terminated and although investigators obtained the software product, it unfortunately did not meet the surveillance needs very well. Investigators shifted emphasis to a program called ESSENCE, sponsored by the DoD Global Emerging Infections Surveillance (GEIS) program. No abstract is available.

### Detail Summary Sheet

|   |  |                          |
|---|--|--------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/041                 | <b>Status:</b> Completed |
| <b>Title:</b> Is Parent Deployment Associated with Decreased Vaccination Rates in Children Under 18 Months Old? |  |                          |
| <b>Principal Investigator:</b> MAJ Mark D. Harris, MC   |  |                          |
| <b>Department:</b> Preventive Medicine  |  | <b>Facility:</b> MAMC    |
| <b>Associate Investigator(s):</b> MAJ Andrew R Wiesen, MC   |  |                          |
| <b>Keywords:</b> deployment, preventive, soldier, vaccination, children, immunizations, military specific       |  |                          |
| <b>Start Date:</b><br>2/26/2002   | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b>  |

**Study Objective:** To determine whether or not parent deployment is associated with decreased vaccination rates in children under 18 months old.

**Technical Approach:** This is a cross-sectional study. Children who are currently enrolled at MAMC born in July or August 2000 will be identified and records reviewed for compliance with each of three recommended immunizations. CHCS information will be compared to data collected from chart review. Deployment information from Oct 2000 and Oct 2001 on parent/sponsor will be obtained from sponsor's unite S1. Data will be analyzed using logistic regression to obtain Odds Ratios for failure to complete each of the recommended regimens (using deployment dats as a continuous variable), including multiple logistic models to identiy significant covariates.

**Progress:** Results: Children who lived off base were approximately half as likely to have completed their immunization series than those who lived on base. Also, the study child was on average 29% less likely to complete an immunization regimen for every additional child in the family. Finally, children in both regimens were about 8% more likely to complete a regimen for every additional year of sponsor age. Days deployed was not statistically significant for either regimen. Sex of child or sponsor, unit type, marital status and rank were also not statistically significantly associated with likelihood of completing one of the regimens. Conclusions: Less than one-half of the MAMC beneficiaries completed the smallest DCD recognized regimen (331), and only one-third completed the full regimen by 18 months of age. Missing immunizations may not have been given or recorded, or the data may be missing in a small number of cases. Additionally, since the CDC immunization compliance data reflects children ages 2 to 4 years, MAMC numbers may be better later in the children's lives. Key factors identified behind Army children not getting immunized include: living away from support systems, younger sponsor/parent age, and larger families. A complete abstract is available.

### Detail Summary Sheet

|                        |                        |                          |
|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/054 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** Is Bupropion a More Effective Smoking Cessation Aid than the Nicotine Patch in the Ft. Lewis Populations?

**Principal Investigator:** CPT Robert J. Newsom, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** LTC James E. Cook, MC

**Keywords:** tobacco, smoking, cigarettes, zyban, military, nrt, nicotine patch

**Start Date:**  
3/26/2002

**Est. Completion Date:**  
Mar 02

**Periodic Review:**

**Study Objective:** To determine if bupropion is more effective therapy than the nicotine patch in our population of cigarette smokers.

**Technical Approach:** Examine the 1 year quit status of 542 consecutive patients that attended at least one tobacco cessation class through Madigan Army Medical Center from Aug 1999 to Sep 2000 using logistic regression to determine if those taking bupropion have a statistically higher quit rate than those patients given the nicotine patch. Age, sex and other routine demographics data will be controlled for as possible confounders.

**Progress:** This study found no statistically significant difference in the 1-year cessation rates among those patients prescribed bupropion or nicotine patch. This finding was consistent regardless of whether the analysis included the non-responders, coded as failures by default, or if the analysis was limited to the responders. In the analysis of the responders only, age was not significantly associated with a successful cessation attempt, but in the subsequent analysis of all the patients coding all non-responders as failures, increasing age was predictive of a successful cessation attempt. In this instance age was likely a marker for multiple attempts at trying to stop using tobacco. The major limitation of this study was the 62.6% response rate. A completed abstract is available.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/121

**Status:** Ongoing

**Title:** The Effectiveness of the Accession Physical Examination and the Military Medical Waiver Process in Identifying Army Officers at Risk for Future Disability

**Principal Investigator:** LTC James D. Terrio, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** LTC James E. Cook, MC; MAJ Andrew R Wiesen, MC; William E. Daniell, M.D., MPH; Joel Kaufman, M.D., MPH

**Keywords:** medical waivers disability pre-employment evaluation early medical discharge

**Start Date:**

9/24/2002

**Est. Completion Date:**

May 03

**Periodic Review:**

**Study Objective:** This project is intended to determine if cadets who receive waivers for medically disqualifying conditions are at increased risk for subsequent disability and identify diagnosis specific, waiverable, medical conditions that increase the risk of medical disability.

**Technical Approach:** Cadets who received waivers for medically disqualifying conditions for ROTC Advanced Camp 1997 and 1998 will be identified using a data base designed to track speciality consults. The database contains name, SSN, age, sex, race, examining speciality clinic, diagnosis and medical disposition. Controls will be identified through a Composite Healthcare System (CHCS) query, which identifies cadets who underwent a physical examination at MAMC and were found to be fully medically qualified. Demographic data will be obtained from the Defense Eligibility Enrollment System (DEERS). Individual identifiers will be used to link with other databases. The time a study subject spends on active duty will be obtained through the Defense Manpower Data Center (DMDC). The DMDC provides data on individuals entering and exiting military service. From this information the length of service can be determined for any individual service member. The DMDC also provides information on branch of military service and the inter service separation code which will identify the reason for military discharge. Hospitalization data on the cohort will be obtained through the U.S. Army Patient Administration System and Biostatistics Activity (PASBA). The PASBA provides hospitalization data on a yearly basis for all active duty soldiers admitted to military hospitals. Information on each admission includes SSN, for linking with other databases, age, gender, race, admission diagnosis, date of disposition, sick days, bed days and outcome. The disability data will be obtained through the Army Physical Disability Agency (APDA). The APDA provides information on all disability cases being considered. For individuals receiving a disability discharge, medical condition codes and degree of disability are also included.

**Progress:** Approval received 28 SEP 02. No data collection yet.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 200/053      **Status:** Completed

**Title:** Using Readily Available Data to Monitor and Surveil Active Duty Injury Occurrence

**Principal Investigator:** MAJ James S. Wadding, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** LTC James D. Wells, MC; CPT Ryung Suh, MC; COL Jeffrey D. Gunzenhauser, MC

**Keywords:** profile, injury, readiness

**Start Date:**  
3/28/2000

**Est. Completion Date:**  
May 00

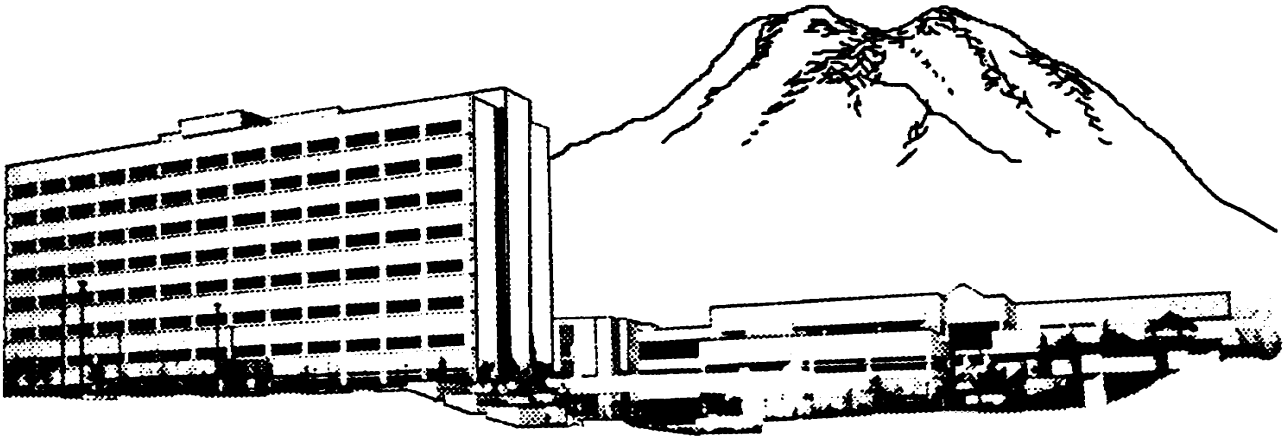
**Periodic Review:**  
1/31/2002

**Study Objective:** To determine if CHCS data can be used to predict loss of readiness due to injury and musculoskeletal illness (in the form of temporary profiles) and to aid in identifying problem areas and possible prevention opportunities on a recurring and real-time basis.

**Technical Approach:** This study is a pilot retrospective cohort study of the frequency and rates of key medical events related to injury occurrence in soldiers. A descriptive analysis of these events will provide thoughtful insight into the magnitude of morbidity typically severe enough to warrant lost-duty time. By looking at records of "sentinel" medications and clinic visits (entries in CHCS which predict the presence of injury or musculoskeletal illness) in CHCS) this study will evaluate the approximate lost time in a military population due to injury. Incidence of injury and illness will be verified by looking at the Standard Installation/Division Personnel Database (SIDPERS). Compiled data from random record selection will provide a profile of military readiness with regard to musculoskeletal injury and lost time due to injury.

**Progress:** This study was completed, Jan 02. 10.5% (n = 4363) of the 41,592 soldiers assigned to Fort Lewis during the 40-month study period met the case definition, and the accumulation of cases appeared to be uniform over time. This is beneficial because as we progress to developing a metric for surveillance, we will be able to look at shorter time periods, eg, 3- or 6- months, and still obtain a reliable estimate of the true population rate. While our case definition includes substantial variation in possible clinic-drug combinations (36), some common themes emerge: 1) Physical Therapy and Orthopedics were the most frequently used clinics among both cases and the population as a whole, and 2) Ibuprofen and other non-steroidal anti-inflammatory drugs accounted for the majority of drug prescribing in both groups. Compared to other Fort Lewis soldiers, cases were more likely to be: female; older, especially in the 30-39 y/o age group; African-American; less-educated, with a considerable proportion having less than a high school degree at study entry; enlisted, especially higher ranking enlisted personnel E5-E9 (Sergeant to Command Sergeant Major); and to be assigned to Combat Support or Combat Service Support trains. Our finding that females were more common among cases compared to the overall population is consistent with prior military and civilian studies that indicate injury rates in women are higher than men after controlling for exposure (given that the Army is representative of one conglomerate working population). Bell et al. has suggested that this may not be purely a function of gender; rather, it may instead be related to underlying current physical fitness, particularly cardiovascular fitness. The finding that higher-ranking enlisted soldiers are over-represented among cases compared to the overall population is not unusual in itself; this is typically considered an age-related effect. Interestingly, there does not appear to be a similar effect among higher-ranking officers, which would be expected if age were the only explanation. Multivariate analysis will be carried out in ongoing studies to further investigate this relationship. After this descriptive part of our study, we believe that the data sources used in this study have the potential to monitor injury 'outbreak' information of importance to commanders and to measure the impact of injury on health care cost and utilization of interest to medical planners. A major strength of our study is the use of

a large cohort over a long period of observation. While it did take a substantial amount of work to assemble the data sets for this 40-month period, especially the SIDPERS information, we would like to remind the reader that we intend for this to be used routinely on a monthly or, at most, quarterly basis. We feel confident at this point that Preventive Medicine Officers should be able to capture, in near real-time, injuries with a significant impact on soldier readiness and health care utilization. Potential limitations of our study include: 1) missing data - the presence of any missing data has the potential to introduce bias. We were uncertain at the beginning about the quality of demographic information we would obtain from SIDPERS. However, missing data really did not appear to be a substantial problem for this portion of our study, with most demographic breakdowns resulting in less than one percent missing or unknown information; 2) proxy measures for injury - The primary underlying assumption of our study is that some temporal sequence of clinic visits and drug prescriptions correlates with an injury substantial enough to restrict work. We hope that the next part of our study which will correlate clinical information with profiles (actual lost-duty time) will help alleviate our concerns with respect to both; and 3) conceptual abstraction - though easy to use and adaptable to changes within CHCS, the proxy measures used for surveillance are difficult to grasp conceptually. This may make it a "difficult sell" to unit commanders who typically yearn for hard numbers and may limit its usefulness on a routine basis. However, commanders are likely to be receptive to timely information if we are able to detect trends early and provide useful feedback and recommendations.



## **Detail Summary Sheets**

### **Department of Psychology**

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/138                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Evaluation of the Field Deployable Record - Behavioral Health   |  |                                      |
| <b>Principal Investigator:</b> LTC Gregory A. Gahm, MS  |  |                                      |
| <b>Department:</b> Psychology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> 1LT Richard Barton, MS; LTC David W. Hough, MC; LTC Reginald Howard, MS; Jessica C. Oehlrich, RA; Deland Peterson, Ph.D.; |  |                                      |
| <b>Keywords:</b> Electronic health computerized patient record telemedicine behavioral health psychology, military specific                                 |  |                                      |
| <b>Start Date:</b><br>10/23/2001  | <b>Est. Completion Date:</b><br>Dec 01 | <b>Periodic Review:</b><br>7/22/2002 |

**Study Objective:** Implement the Field Deployable Record-Behavioral Health electronic record system in garrison and deployment environments, evaluate the FDR-BH on completeness, usefulness, functionality, and user-friendliness, and support clinical implementation studies utilizing this information system.

**Technical Approach:** Twenty providers from Madigan Army Medical Center's Psychology and Psychiatry departments will use this system to record their patients' behavioral health record data. Using a survey design, subjects' demographic data, computer use, and documentation and workload history will be assessed. Every two weeks, providers will rate the overall system on completeness, usefulness, ease of use and functionality as well as specific ratings of the history and encounter documentation sections. After the six-week study period, total documentation time, workload accounting, and accurate session documentation will be measured by documentation time as calculated by the FDR-BH, ADS/KGADS completion, and ratings by independent reviewers respectively. Successful implementation and execution of this FDR-BH protocol, in combination with its Internet and PDA capabilities will support future research initiatives.

**Progress:** A total of 11 behavioral health providers are testing the Field Deployable Record-Behavioral Health. This study remains ongoing at MAMC.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/105 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Telemental Health / Electronic Neuropsychology (e-NP)

**Principal Investigator:** LTC Gregory A. Gahm, MS

**Department:** Psychology

**Facility:** MAMC

**Associate Investigator(s):** CPT Rhonda Koch, MS; LTC Bruce E Crow, MS;

**Keywords:** neuropsychology, telemedicine, Electronic Neuropsychology (e-NP), computerized testing, behavioral health, mental health, psychology

**Start Date:**

6/27/2000

**Est. Completion Date:**

Jul 01

**Periodic Review:**

6/18/2002

**Study Objective:** (1) Evaluate ability of the ANAM2001, a computerized battery of cognitive assessment measures, to serve as a screening instrument for neuropsychological evaluations, (2) Establish infrastructure, procedures, and policies at MAMC to support an Army electronic neuropsychology service (e-NP), (3) Implement a secure server delivery platform for the ANAM2001 and demonstrate its functionality and (4) Explore the modification of ANAM2001 for true internet enabling.

**Technical Approach:** Patients who consent to participate in this study will, following their signing of the consent form, be assigned a case number. The case number will be input in place of the patient's name and SSN for all subsequent information gathering. Case system code will be consistent with the system under development at WRAMC for computerized neuropsychological reporting. This system identifies the test location, in this case MAMC, along with a new sequential 7 digit number. Thus the first subject would be MAMC0000001. Study subjects will complete a computerized history questionnaire containing pertinent questions regarding their background. Following completion of the questionnaire, a psychometrist (test administrator) will set the patient up with a series of automated neurocognitive measures (ANAM2001). Data from the automated measures will be transmitted to a secure server physically located within MAMC. Subjects will then be evaluated using the traditional neuropsychological evaluation measures utilized within the neuropsychological clinic.

**Progress:** Subject recruitment is proceeding slow and steady, with 21 subjects enrolled. Problems with the VTC connection have resulted in all interviews being completed face-to-face.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/109                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Virtual Primary Care Clinic   |  |                                      |
| <b>Principal Investigator:</b> LTC Gregory A. Gahm, MS  |  |                                      |
| <b>Department:</b> Psychology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Jerald W. Rumph, MC; MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC |  |                                      |
| <b>Keywords:</b> Internet, Primary Care, Prevention, Telemedicine, e-Health, Patient Education                                    |  |                                      |
| <b>Start Date:</b><br>7/25/2000   | <b>Est. Completion Date:</b><br>Mar 01 | <b>Periodic Review:</b><br>6/18/2002 |

**Study Objective:** (1) Develop an internet based primary care related service for implementation into the APCC, (2) Determine costs/feasibility of implementing functions as outlined in the original proposal and subsequent Statement of Work, and (3) Develop sub-protocol(s) for IRB approval for patient utilization study using the internet services with complete impact statements.

**Technical Approach:** This study will establish a prototype Virtual Clinic (VC) which will be designed to handle many of the administrative aspects of the APCC. Specific functional options for the VC will be documented and costs for development will be determined. The cost for the various options will be documented and decisions regarding function implementation will be made. A functional model will be operational by 01 January 2001, with data being gathered from January to March 2001. Information about subject interactions with the VC will be ready on the final reporting date of 05 March 2001.

**Progress:** This protocol supported the development of the VPCC. The Applied Research Protocol essentially assumed this project once it was approved. This auxiliary protocol will remain ongoing until the VPCC Applied Research protocol is also completed.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/071 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Virtual Primary Care Clinic - Applied Research

**Principal Investigator:** LTC Gregory A. Gahm, MS

**Department:** Psychology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; CPT Patricia A. McKay, MC; LTC Fujio McPherson, AN; Deland Peterson, Ph.D.; CPT Richard Reed, MC; MAJ Jerald W. Rumph, MC; LTC Mary A. Schwenka, AN; LTC Gary A. Wheeler, MC; COL Nancy A. Woolnough, AN

**Keywords:** Internet, Primary Care, Prevention, Telemedicine, e-Health, Patient Education

**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Aug 01

**Periodic Review:**  
8/14/2002

**Study Objective:** (1) Implement a “virtual” primary care clinic (VPCC) e-health service within the APCC, (2) Determine full range of costs for implementing this program and document usage, (3) Evaluate the impact of these services on patient and provider satisfaction, clinic productivity and workload and (4) Support clinical implementation studies utilizing this clinic, measure impact upon clinical outcome, and project component impact.

**Technical Approach:** This project will implement an e-health VPCC within the APCC at MAMC, which will support a range of patient and provider support that can augment the present access and nature of patient care. Evaluation within this project includes the technical and functional components associated with the VPCC development, impact on patient and provider satisfaction and health system interactions. This VPCC protocol serves as the basic protocol upon which subsequent protocols are linked and describes the basic functionality of the VPCC which is necessary for the other studies implementation.

**Progress:** This protocol is a wrap-around protocol that has supported the submission of other protocols that utilize the Virtual Clinic to support their projects. Subjects have been enrolled in the other protocols and those studies are ongoing.



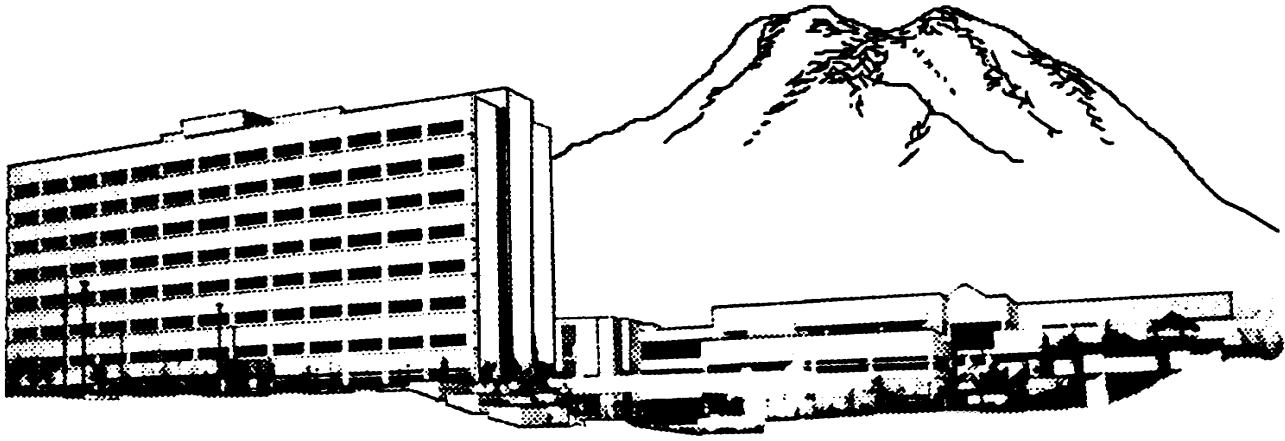
### Detail Summary Sheet

|  |  |                                     |
|--|--|-------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/079                 | <b>Status:</b> Terminated           |
| <b>Title:</b> Primary Care Outpatient Management of Depression Using Internet Technology (VPCC Substudy) |  |                                     |
| <b>Principal Investigator:</b> Deland Peterson, Ph.D.  |  |                                     |
| <b>Department:</b> Psychology  | <b>Facility:</b> MAMC                  |                                     |
| <b>Associate Investigator(s):</b> LTC Gregory A. Gahm, MS; LTC Fujio McPherson, AN;                      |  |                                     |
| <b>Keywords:</b> E-Health, Primary Care, Psychology, Nursing, Telemedicine, Health Promotion             |  |                                     |
| <b>Start Date:</b><br>3/27/2001  | <b>Est. Completion Date:</b><br>Jan 02 | <b>Periodic Review:</b><br>2/6/2002 |

**Study Objective:** (1) Implement an e-health based primary care depression treatment protocol, (2) Evaluate the treatment effectiveness of e-health augmentation of primary care provider's treatment of depression, (3) Evaluate the workload requirements and appropriateness of having primary care providers to include nurse practitioners and primary care physicians working in collaboration with a clinical psychologist to implement supportive psychotherapy into this process, (4) Identify the use and potential role of complimentary/non-traditional medical practices among patients with depression, (5) Evaluate patient satisfaction with this system and (6) Evaluate provider satisfaction with this system.

**Technical Approach:** Patients will be provided with, and asked to sign, an information sheet that describes the study and the requirements on the patient. The will have the opportunity to ask questions of the PI. Patients suffering from depression and eligible for enrollment in VPCC will be assigned to three groups, one with health psychology augmentation of the VPCC primary care team, one being treated by a VPCC primary care team, and one being treated by usual primary care. They will be assessed before initiating treatment and at the conclusion of the VPCC treatment period with the Zung depression scale, a scale measuring their use of alternative treatment methods, and the SF-36v2 health status scale. They will also regularly provide information on sleep quality, use of exercise, and medication usage throughout the treatment period. At the conclusion of this study, information on medical visits and satisfaction with treatment will be collected. Anticipated improvements with treatment progress, resource use and satisfaction with treatment will be evaluated.

**Progress:** This study was terminated by the principal investigator prior to subject enrollment.



**Detail Summary Sheets**

**Department of Radiology**

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/117                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging  |  |                         |
| <b>Principal Investigator:</b> LTC Antonio G. Balingit, MC   |  |                         |
| <b>Department:</b> Radiology   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> CPT Deborah E. Floyd, MS; Jerome Billingsley, M.D.; Jane Besich-Carter, BCNP   |  |                         |
| <b>Keywords:</b> Radioiodinated iodomethynorcholesterol (NP-59) adreno cortical disorders radionuclide scintigraphy  |  |                         |
| <b>Start Date:</b><br>9/24/2002  | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> Clinical evaluation of NP-59 as a diagnostic agent for the detection of adreno-cortical disorders  |  |                         |
| <b>Technical Approach:</b> The drug to be used in this study, NP-59, is investigational and will be used under IND number 12605, which is held by the University of Michigan. This study will be performed in humans of either sex only after complete evaluation by the Endocrinology Service of MAMC. All female patients between the ages of twelve and fifty-five will have a serum B-HCG determination except those who had a hysterectomy. Pregnant or lactating patients will be excluded. This agent will be administered to children less than 18 years of age only for exceptional reasons with the approval of the Chief, Nuclear Medicine Service and Chief, Pediatric Endocrinology Service and only after other alternative procedures are determined to be inappropriate. Ideally, studies in women of childbearing capability are performed during the first 10 days post-menses. NP-59 will be obtained in pharmaceutical form from the University of Michigan Nuclear Pharmacy. In house quality control, including determination of radionuclidic and radiochemical purity, will be performed on all shipments of NP-59 prior to human use. NP-59 will be administered by slow intravenous injection with a dose of 2mCi in adults, 15 UCi/kg in children except where the benefit to risk ratio warrants a higher dose. Under no circumstances will more than 2.2 mCi be administered. Lugol's solution, 5 drops twice daily starting one day before injection and continuing for two weeks, will be used to block thyroid uptake of radionuclide. Planar and SPECT images will be obtained on the 3rd, 4th and 5th days after injection using a dual detector scintillation camera connected to an on-line computer. Studies will be performed in accordance with the protocol "131 I-6-B iodomethylnorcholesterol." Informed consent will be obtained prior to entry into the study. |  |                         |
| <b>Progress:</b> Protocol just recently approved. No patient accrual has been made.  |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/088 | <b>Status:</b> Completed |
|------------------------|-----------------------|--------------------------|

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**Title:** Comparison of Computed Tomography Angiography and Digital Subtraction Angiography for the Pre-Operative Evaluation of Carotid Artery Disease

**Principal Investigator:** CPT David M. Danielson, MC

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|------------------------------|-----------------------|
| <b>Department:</b> Radiology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT David M. Keadle, MC; CPT Christopher R. Spence, MC; MAJ Sean P. Murray, MC; LTC Stephen M. Yoest, MC; James H. Timmons, MD; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Troy H. Patience, B.S.

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**Keywords:** computed tomography, angiography, carotid artery, atherosclerosis, carotid endarterectomy, ultrasound

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**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Jul 00

**Periodic Review:**  
1/22/2002

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**Study Objective:** To evaluate the accuracy of Computed Tomography Angiography (CTA) in the evaluation of patients with atherosclerotic carotid artery disease. Comparison will be made with the with the accepted gold standard evaluation, digital subtraction angiography.

**Technical Approach:** The study sample will be obtained from consecutive patients who have had clinical evaluation and a duplex ultrasound examination in the vascular surgery clinic and who were referred for conventional angiographic examination of the carotid arteries. The plan is to evaluate 40 patients, although a preliminary statistical analysis will be performed after the first 20 patients to assure adequate sample size. Patients who agree to participate in the study will have CTA performed at least 72 hours prior the conventional angiography. These studies will be read by two radiologists. Conventional angiography will then be performed and will be read by two different radiologists. The physicians performing and reading the angiogram will be blinded to the results of the CTA study. Percent stenosis of the carotid artery will be computed using the North American Symptomatic Carotid Endarterectomy Trial method. The results of the CTA will be compared with the conventional angiogram using paired T-test analysis.

The CAT scan protocol used for the CTA exams is as follows: a non-contrast scan will be done first from the skull base to the aortic arch. These will be true axial images at 5 mm slice thickness and intervals using settings of 120 kV and 200 niA. Next, a contrast-enhanced study will be performed. 125 ml of non-ionic contrast material will be injected at a rate of 4ml per second. During the dynamic administration of this contrast material, a scan will be performed from the skull base to the aortic arch. These images will be acquired helically with a pitch of 2 and a slice thickness of 3 mm, and will use settings of 120 kV and 250 mA. These images will be reconstructed at 1 mm thickness, and will be reformatted in sagittal and coronal planes. In addition, 3 dimensional and maximum intensity projection (MIP) images will be obtained. The projected CT weighted dose (weighted 2/3 peripherally and 1/3 centrally) is 9.78 mGy for the contrast scan and 14.76 mGy for the non-contrast scan.

If the ultrasound and the CTA show only unilateral disease, the angiogram on the contralateral side will be abbreviated and will consist of only one contrast run as opposed to three. This will decrease the catheter time in that artery, which is suspected to decrease the chance of stroke. In addition, the decrease in radiation from excluding the two runs will likely exceed the extra radiation from the CTA.

**Progress:** 23 subjects enrolled in this study at MAMC. All data has been collected and is now being evaluated, and reviewed. An abstract of findings is not yet available.

### Detail Summary Sheet

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|---|---------------------------------------|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 98/034                 | <b>Status:</b> Completed             |
| <b>Title:</b> Computed Tomography Guided Percutaneous Placement of Injection Coils Ligated to Suture and Thoracoscopic Pulmonary Resection  |                                       |                                      |
| <b>Principal Investigator:</b> CPT Carl Decker, MC  |                                       |                                      |
| <b>Department:</b> Radiology  | <b>Facility:</b> MAMC                 |                                      |
| <b>Associate Investigator(s):</b> CPT John P. Reinschmidt, MC; MAJ Lawrence M. Casha, MC; MAJ Sean P. Murray, MC; MAJ David P. Tracy, MC; James H. Timmons, MD; MAJ Scott C. Williams, MC; LTC Maceo Braxton Jr, MC   |                                       |                                      |
| <b>Keywords:</b> Video-Assisted Thoracic Surgery, vascular coils, thorascopic lung biopsy   |                                       |                                      |
| <b>Start Date:</b><br>12/18/1997  | <b>Est. Completion Date:</b><br>Indef | <b>Periodic Review:</b><br>1/22/2002 |
| <b>Study Objective:</b> The primary objective is to reduce the number of displaced localization devices by the use of a Cook helical coil tied to a suture line as an alternative to the hookwire for VATS. A secondary objective is to reduce damage that occurs with displacement of wires.   |                                       |                                      |
| <b>Technical Approach:</b> Twenty patients already slotted for needle localization with Hawkins III wires will have either coils attached to suture or hookwires placed. They will then be taken to the OR and thoracic surgery will remove the coils or hookwires with VATS. The degree of displacement and associated complications will be compared to our current 90% Hawkins III wire displacement rate. |                                       |                                      |
| <b>Progress:</b> No subjects enrolled in FY02, for a total of 17 subjects (10 microcoil, 7 hookwire) enrolled at MAMC. There were no adverse events associated with this study. This protocol has ceased to enroll subjects. An abstract of findings is not yet available.  |                                       |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/069 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Cevimeline in the Treatment of Xerostomia Secondary to Radiation Therapy for Cancer in the Head and Neck Region, Protocol Number 2011A-PRT0004

**Principal Investigator:** LTC John B. Halligan, MC

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| <b>Department:</b> Radiology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC William B. Reece, MC; MAJ Douglas M. Sorensen, MC; Ford, Carol D. RN, BSN

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**Keywords:** cevimeline xerostomia radiation therapy cancer

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**Start Date:**  
5/28/2002

**Est. Completion Date:**  
Jun 03

**Periodic Review:**

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**Study Objective:** To evaluate the efficacy of cevimeline at a dose of 30 mg TID with possible escalation to 45 mg TID when compared with placebo upon the subjective global evaluation of dryness of the oral cavity in subjects with xerostomia secondary to radiation therapy for cancer in the head and neck region. To assess the safety of cevimeline, administered at a dose of 30 mg or 45 mg TID, in subjects with xerostomia secondary to radiation therapy for cancer in the head and neck region. To evaluate the efficacy of cevimeline at different doses when compared with placebo on salivary flow and other symptoms associated with xerostomia secondary to radiation therapy for cancer in the head and neck region.

**Technical Approach:** This is a randomized, double-blind, placebo controlled study to evaluated the safety and efficacy of cevimeline compared to placebo in relieving the symptoms of xerostomia secondary to radiation therapy in patients treated for head and neck cancer. Efficacy will be measured subjectively with quality of life questionnaires and objectively with salivary flow tests

**Progress:** This study opened in Sept 02. A total of 4 patients have been enrolled in this study at MAMC during FY02. The four are receiving study treatment. No patients withdrew prior to screening or receiving study drug and one patient was a screen failure (on a medication prohibited by the study). No patient in the study has died. Patient accrual and follow-up will continue during FY02. The anticipated closure date for the study is Dec 31 2002.

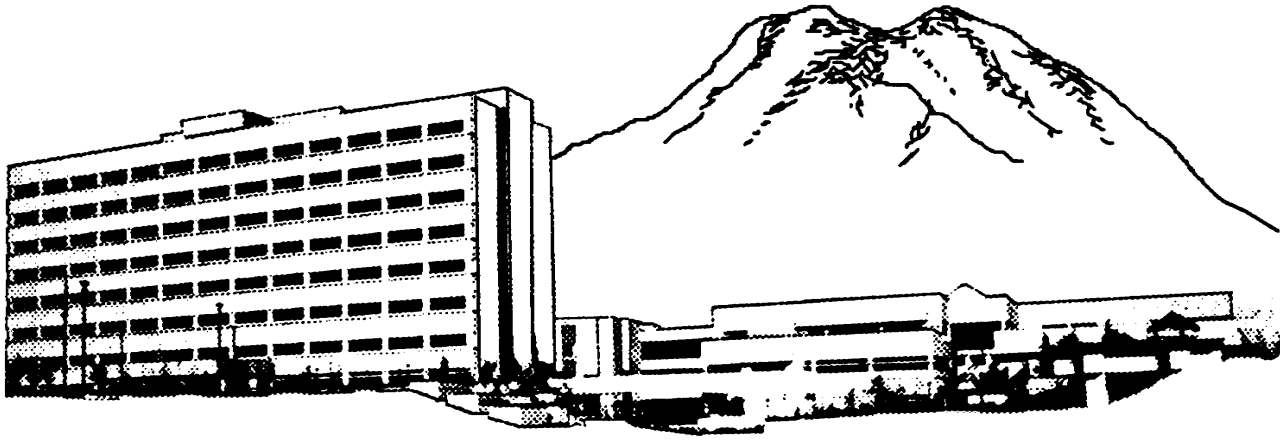
### Detail Summary Sheet

|  |  |                         |
|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/109                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Magnetic Resonance Spectroscopy for Early Evaluation of MS of the Brain  |  |                         |
| <b>Principal Investigator:</b> Frederick C. Stebner, M.D.  |  |                         |
| <b>Department:</b> Radiology   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> LTC Stephen M. Yoest, MC; CPT Shawna E. Scully, MC; CPT Adam J. Benson, MC; LTC Marybeth A. Grazko, MC |  |                         |
| <b>Keywords:</b> MR spectroscopy, multiple sclerosis   |  |                         |
| <b>Start Date:</b><br>8/27/2002  | <b>Est. Completion Date:</b><br>Jul 03 | <b>Periodic Review:</b> |

**Study Objective:** To determine whether performing MR Spectroscopy in addition to MRI of the brain adds prognostic value in the early diagnosis of optic neuritis and multiple sclerosis

**Technical Approach:** This study is a prospective, observational protocol. Patients referred for MRI evaluation of the brain for suspected MS will also have a MR spectroscopy study performed. Patients will be followed until a clinical diagnosis is made. This will be done by prospective chart review or consultation with the patient's clinical physician. If the diagnosis of MS or optic neuritis is made, then these patients will be followed after therapy is started to evaluate response or progression. This study plans to follow patients at six (6) to twelve (12) month intervals for approximately two (2) years.

**Progress:** This study recently received IRB approval and has not yet been initiated at MAMC.



## **Detail Summary Sheets**

### **Department of Surgery, Opthamology**



## Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/122                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Double-Blind, Randomized, Placebo-Controlled Study to Assess the Efficacy and Safety of Circulase for the Treatment of Critical Leg Ischemia, Protocol WFI 01-01  |  |                                      |
| <b>Principal Investigator:</b> Charles A. Andersen, M.D.  |  |                                      |
| <b>Department:</b> Surgery  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC Dennis Febinger, MC; CPT Philip S. Mullenix, MC; LTC Neal C. Hadro, MC; MAJ Benjamin W. Starnes, MC   |  |                                      |
| <b>Keywords:</b> ABI-Ankle Brachial Index, CLI-Critical Leg Ischemia, ECG-Electrocardiogram, TBI-Toe Brachial Index, QOL-Quality of Life  |  |                                      |
| <b>Start Date:</b><br>7/24/2001   | <b>Est. Completion Date:</b><br>Oct 02 | <b>Periodic Review:</b><br>6/25/2002 |
| <b>Study Objective:</b> To test the hypothesis that Circulase treatment improves clinical outcome by reducing the risk of major amputation in subjects with critical leg ischemia who have undergone a recent peripheral revascularization procedure.   |  |                                      |
| <b>Technical Approach:</b> Patients will be randomized to one of two double-blinded treatment groups-Circulase 40 mg or Placebo The total goal for enrollment is 6-10 patients here at MAMC. Informed consent will be obtained by one of the investigators or by one of the study coordinators. They will verbally explain the study purpose and requirements. After all questions have been answered, the patient will be instructed to read, sign and date the consent in the presence of a non-study related witness The patient will then enter the screening phase, which will last 10 days The following assessments will be performed: Medical history, Physical examination, Electrocardiogram, Peripheral vascular intervention history, Assessment of critical leg ischemia (presence of ulcers or gangrene, ischemic rest pain, hemodynamic status assessment, ABI's, wound tracings and photographs), Neuropathy assessment, QOL measurements (SF-36, Pain VAS), Concomitant medication assessment, Urine and Laboratory measurements. After verification of patient eligibility based on inclusion/exclusion criteria the patient is eligible to be randomized. Within a 24 hours of the planned revascularization procedure the study coordinator will contact the ClinPhone Interactive Voice Response system (IVRS) to assign the next available subject number. Test administration procedures should begin within 24 hours the revascularization procedure, unless contraindicated by the Investigator. Test material may be delayed, up to 3 days from the date of randomization if a clinically significant condition is present, which in the investigators opinion poses a safety risk. The test material should be initiated as soon as the patient is stabilized. If the patient is unable to initiate the test material within 3 days they will be withdrawn from the study. After dosing the patient will be monitored for all adverse events and the administrator will assess the severity and risk to the patient and will administer medical treatment to alleviate symptoms for hemodynamic stability. Before releasing the patient from the hospital the investigator will provide a detailed post-operative description of the revascularization procedure. A total of 40 test material administrations are to be performed over the 56 day dosing period. The patient will receive study infusion in the vascular clinic during work week. In the event that home healthcare is accessible, the patient may receive home infusions at the discretion of the investigator. The investigator will instruct the home health care provider on the protocol, drug administration, and drug pharmacokinetics. All patients will be required to return to the clinic for physical exams and outcome evaluations at week 8, EOT, or if they have an SAE. At each dose the patient will be monitored for all adverse events, concomitant medications, and hemodynamic stability prior to being released from the study site. |  |                                      |
| <b>Progress:</b> A total of 4 patients have been enrolled into this study at MAMC during FY02. Two patients screen failed and 2 patients received study drug. Two patients remain in follow-up. This study is still open to enrollment at MAMC.   |  |                                      |

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/123      **Status:** Ongoing

**Title:** A Double-Blind, Randomized, Placebo-Controlled Study to Assess the Efficacy and Safety of Circulase in Conjunction with Peripheral Revascularization for the Treatment of Critical Leg Ischemia, Protocol WFI-01-02

**Principal Investigator:** Charles A. Andersen, M.D.

**Department:** Surgery      **Facility:** MAMC

**Associate Investigator(s):** LTC Dennis Febinger, MC; CPT Philip S. Mullenix, MC; LTC Neal C. Hadro, MC; MAJ Benjamin W. Starnes, MC

**Keywords:** ABI-Ankle Brachial Index, CLI-Critical Leg Ischemia, ECG-Electrocardiogram, TBI-Toe Brachial Index, QOL-Quality of Life, Index Operation-study-qualifying peripheral revascularization procedure, military specific

**Start Date:**  
7/24/2001

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
6/25/2002

**Study Objective:** To test the hypothesis that Circulase treatment improves clinical outcome by reducing the risk of major amputation in subjects with critical leg ischemia who have undergone a recent peripheral revascularization procedure.

**Technical Approach:** This protocol will be studying male or female patients 40 years or older, with critical leg ischemia after undergoing a distal revascularization procedure. Patients will be randomized to one of two double-blinded treatment groups-Circulase 40 mg or Placebo The total goal for enrollment is 6-10 patients here at MAMC. Upon obtaining informed consent, the patient will enter a 10 day screening phase and the following assessments will be performed: medical history, physical exam, electrocardiogram, peripheral vascular intervention history, assessment of critical leg ischemia (presence of ulcers or gangrene, ischemic rest pain, hemodynamic status assessment, ABI's, wound tracings and photographs), neuropathy assessment, QOL measurements (SF-36, Pain VAS), concomitant medication assessment, urine and laboratory measurements. Patient will already be scheduled to receive a distal revascularization procedure involving an artery beyond the popliteal as part of their normal standard of care. Patients requiring treatment of proximal lesions in conjunction with a described distal procedure are acceptable. After verification of patient eligibility based on inclusion/exclusion criteria the patient is eligible to be randomized. Within 24 hours of the planned revascularization procedure the study coordinator will contact the ClinPhone Interactive Voice Response system (IVRS) to assign the next available subject number. Test administration procedures should begin within 24 hours the revascularization procedure, unless contraindicated by the Investigator. Test material may be delayed, up to 3 days from the date of randomization if a clinically significant condition is present, which in the investigators opinion poses a safety risk. The test material should be initiated as soon as the patient is stabilized. If the patient is unable to initiate the test material within 3 days they will be withdrawn from the study. After dosing the patient will be monitored for all adverse events and the administrator will assess the severity and risk to the patient and will administer medical treatment to alleviate symptoms for hemodynamic stability. Before releasing the patient from the hospital the investigator will provide a detailed post-operative description of the revascularization procedure. Including: Arteriogram showing the patency of the Index Operation in communication with the run-off, Magnetic resonance angiography (MRA) showing the patency of the Index operation, Color duplex scanning showing patency of the Index Operation, and Increase in distal ABI by at least 0.15 over pre-operative ABI. All Test material procedures are performed identically at each treatment visit. A total of 40 test material administrations are to be performed over the 56 day dosing period. At each dose the patient will be monitored for all adverse events, concomitant medications, and hemodynamic stability prior to being released from the study site. At Week 1, the patient will receive a study infusion in the vascular clinic given by a

nurse or a CRC-RN. Prior to the dose being given the patient's blood pressure will be recorded. The patient will be placed in the supine position using an appropriate indwelling catheter, syringe pump and infusion line. The dose will last approximately 10 minutes. Also at this visit an ECG will be done, at least 45 minutes after the start of test material.

The Week 8 visit will occur the last week of treatment (days 50-56) and the following procedures will be performed: Test material procedures (if patient is still receiving treatments), Physical exam, Assessment of critical leg ischemia, Index operation patency surveillance (Arteriogram, Magnetic resonance angiography, Color duplex scanning, and/or Increase in distal ABI by at least 0.15 over pre-operative ABI), Laboratory measurements, QOL measurements (SF-36, VAS), ECG (post drug administration), Neuropathy assessment, Drug Reconciliation (after final dose), Monitoring for all adverse events, concom med's and vascular interventions, Hemodynamic status assessment (ABI's). Following the eight week treatment period and visit the patient will enter the follow-up period. The patient will be contacted by telephone, once a month for the full one year period, to assess AE's and Concom med's. After the 30 day period only serious adverse events will be assessed and reported. Patients will return at months 6 and 12 month. An Exit Visit for those patients that discontinue participation in the study the following procedures will be done. The data collected will be the reduction in the event rate which is defined as the proportion of patients who undergo a major amputation or die within 6 months from the initial treatment. This will be analyzed by logistic regression testing for the drug effect on the event rate while adjusting form the following baseline characteristics: diabetic status, ischemic ulcer/gangrene presence and anti-platelet therapy.

**Progress:** A total of 2 patients have been enrolled into this study here at MAMC during FY02. Two patients received study treatment and are still being followed. This study remains open to enrollment at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/046      **Status:** Ongoing

**Title:** A Pivotal Study to Evaluate the Safety and Efficacy of Cryopreserved Bilayered Cellular Matrix (Cryo-OrCel) for the Treatment of Venous Ulcers Protocol #100-VLU-01-CLN

**Principal Investigator:** Charles A. Andersen, M.D.

**Department:** Surgery      **Facility:** MAMC

**Associate Investigator(s):** COL David F. J. Tollefson, MC; LTC Dennis Febinger, MC; LTC Neal C. Hadro, MC

**Keywords:** venous ulcers, collagen matrix, allogeneic cells

**Start Date:**

1/23/2001

**Est. Completion Date:**

Sep 01

**Periodic Review:**

12/19/2001

**Study Objective:** This is a pivotal study to determine the safety and efficacy of Cryopreserved Composite Cultured Skin (Cryo-CCS) plus standard care compared to standard care alone in the treatment of venous ulcers.

**Technical Approach:** The study is divided into two phases. The initial phase will enroll approximately 12 patients at three centers. This phase will be open label and all patients will receive CCS. After those patients have received up to four applications of CCS, investigators will select and enroll a sufficient number of patients to yield 176 evaluable subjects (8-10 at MAMC) into the randomized phase, which will be an open label, parallel group, randomized study of at least 176 patients enrolled among 35 centers in the United States. The 26-week study consists of four periods: a two-week screening period, a four-week Active period, an eight week Maintenance period, and a three month Follow-up period. All patients will be enrolled for a maximum of 26 weeks. The Initial phase will be an open label phase-in period to further assess the potential for an immune reaction. After a two week trial of standard care, these twelve patients will receive up to four weekly applications of CCS (Active period, Visits 1 to 5). If no safety issues emerge, enrollment may continue in the Initial phase until all 12 patients have been enrolled and treated. Patients in the Initial phase will continue through the Active and Maintenance (Visits 6 to 13) periods. Patients whose ulcers are not healed by visit 13 are considered completed subjects and their study participation is ended. Subjects with complete healing at any point during the study will enter the follow-up period. They will be followed on a monthly basis (every 25 -35 days) for three months from the date of 100% re-epithelialization. Subjects who achieve healing are considered completed subjects if they finish all the required follow-up visits.

The Randomized phase (evaluation of 176 patients) will begin if no device-related adverse events have occurred in the Initial phase which would increase the risk to patients and prevent the discontinuation of the study. Patients are initially evaluated at a screening visit. After meeting the enrollment criteria, (two trial of standard care) patients will be randomized to a treatment group. Patients randomized to the CCS treatment group will receive weekly applications of CCS along with standard care. Patients randomized to the standard care treatment group will receive up to four weeks of standard care alone. Patients in either treatment group who do not achieve healing during the Active period will enter the Maintenance period, which consists of up to eight additional weeks of standard care alone. Patients whose ulcers are not healed by visit 13 are considered completed subjects and their study participation ends. Patients whose ulcers heal completely at any point during the study will enter the follow-up period. They will be followed monthly (every 25-35 days) for three months from the date of 100% re-epithelialization. Patients who achieve healing are considered completed patients if they finish all required follow-up visits.

**Progress:** This study has not yet begun here at MAMC due to sponsor device production problems.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/088                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Prospective, Randomized Study Comparing the Outcome of Carotid Endarterectomy Using New Generation Dacron or Expanded Polytetrafluoroethylene (e-PTFE) Carotid Patching   |  |                                      |
| <b>Principal Investigator:</b> Charles A. Andersen, M.D.  |  |                                      |
| <b>Department:</b> Surgery  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC Stephen B. Olsen, MC; COL David F. J. Tollefson, MC   |  |                                      |
| <b>Keywords:</b> endarterectomy, carotid patching, dacron, e-PTFE   |  |                                      |
| <b>Start Date:</b><br>5/23/2000   | <b>Est. Completion Date:</b><br>Jun 02 | <b>Periodic Review:</b><br>6/25/2002 |
| <b>Study Objective:</b> The primary objective of this study is to compare the performance of the newest generation Dacron and e-PTFE patches with respect to: (1) postoperative stroke/thrombosis, (2) recurrent carotid stenosis and (3) intraoperative handling/blood loss.   |  |                                      |
| <b>Technical Approach:</b> After informed consent, patients will be randomized to patch angioplasty with either a Hemashield Finesse patch or a Gore-Tex Acuseal patch. Surgeons will rank the handling of the patch on an analog scale. Time to cessation of bleeding will be monitored. Patients will have an intraoperative duplex , and follow-up duplex examinations at 3, 6, 9, 12, 18 and 24 months after the operation. Rates for carotid restenosis will be determined. Perioperative and late neurologic morbidity will be identified and determined. |  |                                      |
| <b>Progress:</b> A total of 35 patients have been enrolled into this study here at MAMC, with 15 patients enrolled since Oct 01. One patient screen failed and 34 patients received study treatment. All 34 patients remain in follow-up and this study is still open to enrollment during FY02.  |  |                                      |

### Detail Summary Sheet

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|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 96/163 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** Clinical Evaluation of the Handling and Performance of the HEMASHIELD Knitted Double Velour Fabric and Polytetrafluoroethylene (PTFE) Patched for Carotid Endarterectomy Patch Procedures in Patients

**Principal Investigator:** Charles A. Andersen, M.D.

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|----------------------------|-----------------------|
| <b>Department:</b> Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Edmund A. Kanar, M.D.; George J. Collins, Jr., M.D.

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**Keywords:** Carotid endarterectomy, HEMASHIELD

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**Start Date:**  
9/20/1996

**Est. Completion Date:**  
Nov 98

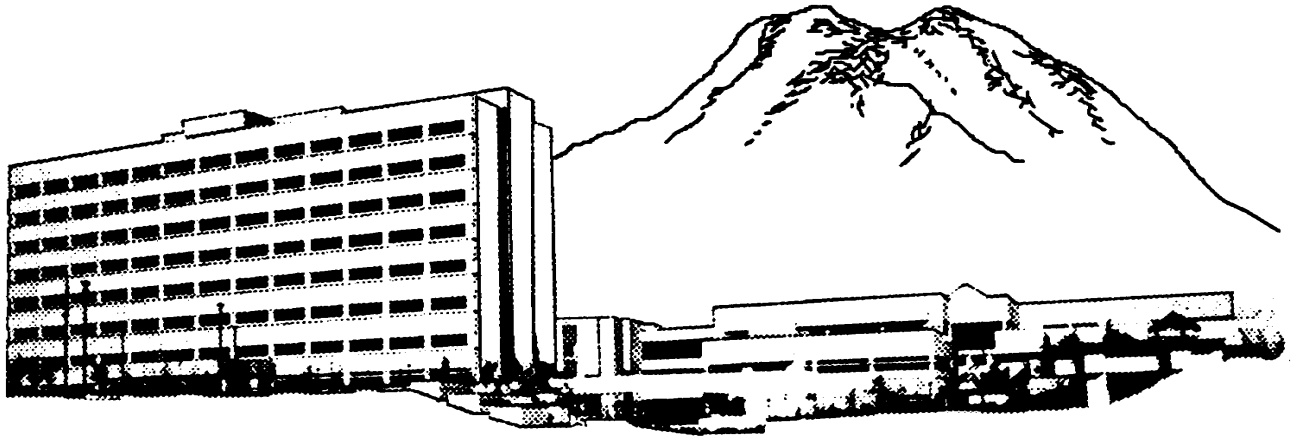
**Periodic Review:**  
8/8/2002

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**Study Objective:** The objective of this randomized, parallel group, multi-center study is to evaluate the performance of the test product, the HEMASHIELD® Knitted Double Velour patch in comparison to the control product, the Gore-Tex patch, for use as a carotid artery patch following carotid endarterectomy in patients.

**Technical Approach:** This is a prospectively randomized, multi-center clinical trial in which a maximum of 40 patients will be enrolled, with approximately equal numbers of patients in each of the 2 treatment groups, Hemashield patch vs. the Gore-Tex patch. Anticipated MAMC enrollment is approximately 20 patients. Patients included in this study will be evaluated preoperatively, intraoperatively, at discharge from the hospital, and at 3 months, 6 months, 12 months and up to a total of 24 months postoperatively. Follow-up evaluations will include a medical history and physical exam at 3, 6, 12 and 24 months and duplex ultrasound testing at 6 and 12 months (with optional duplex scan at 24 months) for assessment of patch repair. Completion of follow-up assessment and final report is anticipated about one and one half years after the first patient enrollment.

**Progress:** This study enrolled 40 patients at MAMC, 3 of which were seen failures. 37 patients received study treatment. This study is closed to enrollment. All patient follow up has been completed during FY02 and the sponsor is in the process of closing this study out.



## **Detail Summary Sheets**

### **General Surgery Service, Department of Surgery**

## Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/142                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Prospective, Randomized, Double-blind, Multicenter Trial Assessing the Safety and Efficacy of Sequential (intravenous/oral) BAY 12-8039 (moxifloxacin) 400 mg every 24 hr Compared to Intravenous Piperacillin/Tazobactam 3.375 gm every 6 hr Followed by Oral Amoxicillin/Clavulanic Acid Suspension 800 mg every 12 hr for the Treatment of Patients with Complicated Intra-abdominal Infections  |  |                                      |
| <b>Principal Investigator:</b> LTC Kenneth S. Azarow, MC  |  |                                      |
| <b>Department:</b> Surgery/General Surgery  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC Ronald J. Place, MC; CPT Leroy J. Trombetta, MC; CPT James A. Sebesta, MC; CPT Christopher K. Sanborn, MC; MAJ Matthew J. Martin, MC; CPT Mohamad I. Haque, MC; CPT Scott R. Steele, MC; Margaret I. Voelker, RN, CRC   |  |                                      |
| <b>Keywords:</b> Intra-abdominal infections, peritoneal inflammation, Intra-abdominal abscess, Macroscopic gastrointestinal perforation   |  |                                      |
| <b>Start Date:</b><br>9/26/2000   | <b>Est. Completion Date:</b><br>Feb 02 | <b>Periodic Review:</b><br>9/24/2002 |
| <b>Study Objective:</b> To compare the safety and efficacy of sequential (intravenous/oral) moxifloxacin every 24 hours with the combination of intravenous piperacillin/tazobactam (Zosyn*) every 6 hr followed by oral amoxicillin/clavulanic acid (Augmentin*) suspension every 12 hours for the treatment of adult patients with complicated intra-abdominal infections.  |  |                                      |
| <b>Technical Approach:</b> The primary diagnosis of each patient in this study will be complicated intra-abdominal infection defined as an intra-abdominal infection in which an operative procedure or percutaneous drainage is required for diagnosis and management. Findings at operation must confirm the presence of an intra-abdominal infection (e.g., presence of purulent exudate and inflamed or necrotic tissue).   |  |                                      |
| Patients will be randomized to one of two treatment groups. Treatment Group 1: Experimental treatment arm of Moxifloxacin 400 mg, administered by intravenous infusion over 60-minutes every 24 hours plus a piperacillin/tazobactam placebo infusion every 6 hours. If the patient is switched from intravenous to oral moxifloxacin 400 mg tablet every 24 hours, they will also receive amoxicillin/clavulanic acid placebo suspension every 12 hours.   |  |                                      |
| Treatment Group 2: Standard treatment arm of Piperacillin/Tazobactam 3.375 gm, administered by intravenous infusion over 60-minutes every 6 hours plus a moxifloxacin placebo infusion every 24 hours. If the patient is switched from intravenous piperacillin/tazobactam to oral amoxicillin/clavulanic acid suspension 800 mg every 12 hours, they will also receive a moxifloxacin placebo tablet every 24 hours.   |  |                                      |
| For both treatment groups, at the investigator's discretion, a switch to oral therapy could be made if the following criteria are met; (1) patient is clinically improving on intravenous therapy, (2) gastrointestinal motor activity has returned as indicated by passage of gas or feces per rectum or ostomy or (3) gastrointestinal function is present as indicated by tolerance of enteral feedings, either by mouth or by tube (including jejunostomy). Patients will be evaluated for complete recovery. |  |                                      |
| <b>Progress:</b> During FY02, ten patients were screened but not enrolled, eight patients were enrolled and three were withdrawn early in the study. One MAMC SAE was reported in Jan 02 due to a nonrelated condition. Three associate investigators were added to project in July 02 from surgical resident staff. Study project extended to December 2002.   |  |                                      |



### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/091                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra hircus, Pig/Sus scrofa, and Sheep/Ovis aries)   |  |                         |
| <b>Principal Investigator:</b> LTC Kenneth S. Azarow, MC  |  |                         |
| <b>Department:</b> Surgery/General Surgery  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ L. Layne Norlund, VC; COL William E. Eggebroten, MC; LTC Clifford A. Porter, MC; SFC DiAnn Dansereau, USA   |  |                         |
| <b>Keywords:</b> ATLS, life support, combat or military, trauma or injury, train or teach or educate or instruct, model or method or technique or procedure, military specific  |  |                         |
| <b>Start Date:</b><br>3/14/2001   | <b>Est. Completion Date:</b><br>Feb 04 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> To train federally affiliated (e.g. DoD/VA) HCPs in advanced/combat trauma management skills essential to the maintenance of combat medical readiness. More specifically, this protocol encompasses both formal ATLS certification training, and duty/mission-specific combat-relevant trauma management training that is of limited availability to military HCPs in peacetime practice.   |  |                         |
| <b>Technical Approach:</b> The protocol supports three levels of trauma management training, as follows: 1) Formal Advanced Trauma Life Support (ATLS) training and certification (physicians), recognized and accredited by the American College of Surgeons (ACS). 2) Combat-relevant Trauma Management training for physicians (CTM-P), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 3) Combat-relevant Trauma Management training for ancillary medical personnel (CTM-NP), focusing on "hands-on" training of mission/duty-related trauma intervention procedures selected from levels 1 and 2, above. The animal use portion of ATLS training is strictly defined by the ACS, as described in Section V.A.1., Experimental Design and General Procedures: ATLS. Trauma management training under levels 2 and 3, above, is likewise described in Sections V.A.2. and 3., respectively. Training associated with this protocol will utilize both inanimate (e.g. mannequin, cadaver, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. CTM-NP training (level 3, above) will generally be combined with CTM-P training activities (level 2, above), or will utilize animal cadavers in order to minimize the number of live animals sacrificed in support of this protocol (Eaton BD, et al, 1990). Animal species used for this protocol will include sheep, goat and pig. |  |                         |
| <b>Progress:</b> This training protocol was not used during FY02.   |  |                         |

### Detail Summary Sheet

|                        |                        |                        |
|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/083 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Does the Concentration of Gastrin Releasing Peptide Receptors on the Surface of Human Neuroblastoma Specimens Predict the Aggressiveness of the Tumor?

**Principal Investigator:** LTC Kenneth S. Azarow, MC

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|--|-----------------------|
| <b>Department:</b> Surgery/General Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT James A. Sebesta, MC; Robert S. Sawin, M.D.

**Keywords:** Neuroblastoma, ganglioneuroma, gastrin releasing peptide receptor, GRP

**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Nov 01

**Periodic Review:**  
8/12/2002

**Study Objective:** To evaluate the concentration of Gastrin Releasing Peptide Receptors on the surface of neuroblastoma tissues and correlate this to the aggressiveness of the individual tumor. This potentially could be used as a prognostic tool during the initial evaluation of neuroblastomas.

**Technical Approach:** This study will evaluate 50 tumor specimens using a radioligand to mark each receptor and a gamma counter to determine the number of bound radioligands based on the known activity of the radioactive label. The clinical nature of the tumors will be compared to the receptor density to determine if an increased number of receptors indicates a more aggressive tumor requiring aggressive early therapy.

**Progress:** Final set of experiments to be completed in the next 45 days. Paper pending final data

## Detail Summary Sheet

|   |  |  |  |                         |  |
|---|--|--|--|-------------------------|--|
| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 202/049                 |  | <b>Status:</b> Ongoing  |  |
| <b>Title:</b> Linezolid vs. Vancomycin for the Treatment of Complicated Skin and Soft Tissue Infections Suspected of Being or Proven to be Due to a Methicillin Resistant Gram-positive Bacterial Pathogen (Protocol Number 766-INF-0026-128)   |  |  |  |                         |  |
| <b>Principal Investigator:</b> LTC Kenneth S. Azarow, MC  |  |  |  |                         |  |
| <b>Department:</b> Surgery/General Surgery  |  |  |  | <b>Facility:</b> MAMC   |  |
| <b>Associate Investigator(s):</b> MAJ Matthew J. Martin, MC; CPT Mohamad I. Haque, MC; CPT Scott R. Steele, MC  |  |  |  |                         |  |
| <b>Keywords:</b> Methicillin-resistant Staphylococcus aureus (MRSA); antimicrobial surveillance programs  |  |  |  |                         |  |
| <b>Start Date:</b><br>2/26/2002   |  | <b>Est. Completion Date:</b><br>Mar 03 |  | <b>Periodic Review:</b> |  |
| <b>Study Objective:</b> Primary Objectives: To demonstrate the clinical superiority of linezolid in the treatment of suspected or proven resistant gram positive skin and soft tissue infections when compared to vancomycin or Oxacillin/Nafcillin/Flucloxacillin/ Dicloxacillin if MSSA is identified. The clinical superiority will be determined by higher clinical cure rate of Linezolid over comparators. Principal Secondary Objectives: To demonstrate the economic superiority of linezolid for this patient population, determined by a shorter LOS for linezolid over comparators. Other Secondary Objectives: To evaluate time to normalization of temperature; evaluate lesion size based on the area of erythema and induration; evaluate microbiology outcome. To assess adverse events associated with treatment of skin and soft tissue infections (SSTI).  |  |  |  |                         |  |
| <b>Technical Approach:</b> This is a randomized, open-label, comparator-controlled, and health economic study that will evaluate and compare the clinical efficacy, safety and tolerance, as well as direct medical resource use as measured by length of hospital stay, of two regimens in the treatment of complicated skin and soft tissue infections (SSTI). Patients with complicated skin and soft tissue infections including post operative wound infections who are under care of the General Surgery Service of Madigan Army Medical Center, or patients referred to this service for surgical intervention (e.g., incision and drainage, debridement) and appropriate antibiotic therapy of the infection will be the source of study subjects at MAMC. Patients enrolled will be randomized in the ratio of 1:1 to two treatment arms to receive either Linezolid 600 mg every 12 h or Vancomycin 1 gram every 12 hours. All vancomycin patients will begin their treatment with intravenous study medication. If the patient has documented methicillin-sensitive staph aureus (MSSA), the individual will be switched to Oxacillin sodium/Nafcillin/Flucloxacillin IV (1-2g, every 6 hours), or Dicloxacillin sodium PO (500 mg, every 6 hours) after the initial vancomycin IV therapy. Linezolid patients may receive IV or oral treatment as appropriate. Clinical evaluations will be performed throughout the study period for efficacy and safety assessments. The length of hospital stay will be compared between the two treatment groups. Planned therapy is at least 7-14 days and may be extended for up to 21 days. 500 evaluable patients per treatment group will be recruited, with enrollment of approximately 10 patients at MAMC. Comparability of treatment groups with respect to the categorical variables sex, race, medical history, wound description (wound erythema, drainage, and discharge), diagnosis and clinical signs and symptoms will be assessed using a chi-square test for two-way contingency tables. Statistical tests will be two-sided using P-values less than or equal to 0.05 to determine statistically significant findings. All confidence intervals (CI) will be 95%, and those used with proportional outcomes will be based on a normal approximation to the binomial distribution of success/failure. |  |  |  |                         |  |
| <b>Progress:</b> Protocol recently received approval. No progress to report.  |  |  |  |                         |  |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 202/084      **Status:** Ongoing

**Title:** Linezolid vs Vancomycin/Oxacillin/Dicloxacillin in the Treatment of Catheter-related Gram-positive Bloodstream Infections, Protocol Number M/1260/0080

**Principal Investigator:** LTC Kenneth S. Azarow, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew J. Martin, MC; CPT Mohamad I. Haque, MC; CPT Scott R. Steele, MC; Margaret I. Voelker, RN, CRC; CPT Amy L. Young, DO

**Keywords:** nosocomial infection bacteremia gram-positive pathogens Staphylococcus catheters methicillin susceptible pathogens

**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Nov 03

**Periodic Review:**

**Study Objective:** The primary objective of this study is to compare the microbiological efficacy of linezolid to vancomycin/oxacillin/dicloxacillin in the empiric treatment of patients with gram-positive catheter-related bloodstream infections. Secondary Objectives: Clinical efficacy of linezolid compared to vancomycin/oxacillin/dicloxacillin, Incidence of late metastatic sequelae associated with *S. aureus* infections in patients treated with linezolid or vancomycin/oxacillin/dicloxacillin, Pathogen eradication, Safety and tolerance, Hospital resource use

**Technical Approach:** This is a randomized, open-label, comparator-controlled study of linezolid vs. vancomycin/oxacillin/dicloxacillin in the treatment of male and female patients 13 years or older and weighing  $\geq 40$  kg with catheter-related bloodstream infections caused by gram-positive pathogens. The trial will focus on patients with short-term, nontunneled central venous catheters, pulmonary artery catheters, and arterial catheters in place at least 3 days. Amendment 1 to the protocol issues conditions for inclusion of patients who have tunneled catheters. Patients will be randomized to either the linezolid treatment arm or the vancomycin/oxacillin/dicloxacillin treatment arm. Linezolid will initially be given IV, and may later be switched to oral. Patients in the comparator arm will initially receive IV vancomycin. Those with a methicillin-susceptible gram-positive pathogen may be switched to IV oxacillin and/or oral dicloxacillin. Both treatment groups may also receive open-label antibiotic coverage for gram-negative pathogens. Peripheral and catheter blood samples will be obtained before study medication is initiated. The samples will be cultured in the MAMC laboratory. The infected catheter will be removed and the tip cultured. Exudate and site aspirate will be cultured as available. If a gram-positive organism is not identified from the catheter tip or site aspirate/exudate, the patient will be removed from the study. Isolates of pathogens will be shipped to a central study laboratory for verification. Repeat blood cultures are taken after start of treatment. If still positive by a second recheck, the patient will be withdrawn from the study as a treatment failure. Assessments will be documented at days 3, 7, 14, and 21, and at the End of Treatment (EOT), a Short Term Follow Up 1-2 weeks after EOT. For patients with *S. aureus* bloodstream infection, a Long Term Follow Up visit will be performed at 6-8 weeks after EOT. Clinical efficacy will be measured by improved signs and symptoms. Incidence of metastatic sequelae of *S. aureus* infections will be measured at the Long Term Follow Up. Eradication rates of individual pathogens will be analyzed. Safety and tolerance will be measured by laboratory assay results and adverse event findings including mortality. Hospital resource use will be evaluated by length of stay, hospital discharge rate, and length of antibiotic treatment.

**Progress:** The protocol received final IRB approval September 2002. No patients were enrolled to this study in FY02.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/027                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Efficacy of Rofecoxib in the Treatment of Postoperative Pain after Laparoscopic Cholecystectomy and Inguinal Hernia Repair |  |                         |
| <b>Principal Investigator:</b> CPT Daniel R. Cronk, MC   |  |                         |
| <b>Department:</b> Surgery/General Surgery   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> MAJ Matthew J. Martin, MC; CPT Scott R. Steele, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC |  |                         |
| <b>Keywords:</b> laparoscopic cholecystectomy, hernia repair, rofecoxib, postoperative pain  |  |                         |
| <b>Start Date:</b><br>1/22/2002  | <b>Est. Completion Date:</b><br>Dec 02 | <b>Periodic Review:</b> |

**Study Objective:** Prospectively compare the post-operative pain and oral narcotic requirement following laparoscopic cholecystectomy and hernia repair in a cohort of patients given rofecoxib (vioxx) versus placebo. Evaluate the time of return to duty following laparoscopic cholecystectomy and hernia repair with and without rofecoxib. Determine any difference in perioperative and postoperative complication rates between the rofecoxib and placebo groups. Analyze cost-effectiveness of rofecoxib for post operative analgesia following laparoscopic cholecystectomy and hernia repair.

**Technical Approach:** In this study we will compare the post-operative pain and narcotic use in 34 consecutive patients undergoing laparoscopic cholecystectomy and 34 patients undergoing inguinal hernia repair when using rofecoxib versus placebo for postoperative pain control. We will use a visual analogue scale for patients to quantify their pain pre-operatively and then on days 1, 2, and 5. Post-operative narcotic requirements per 24 hours will similarly be recorded on post-operative days 1, 2, and 5. A post operative history and physical exam will be performed on approximately post operative day 14. Time to return to work or usual activity level will be recorded either at the first postoperative visit or by a follow up telephone call. We will call patients on postoperative day 28 to ensure no further complication. Data will be analyzed using a two-tailed t-test.

**Progress:** A total of 17 patients have been enrolled at MAMC during FY02. One patient was removed from the study because they received an intravenous NSAID dosage as an inpatient, which is a defined exclusion criteria. There have been no adverse effects of the study. Patients will continue to be enrolled during this year and have appropriate follow up. There are no reportable data from this study thus far because not enough patients for an interim analysis have been enrolled.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/118 | <b>Status:</b> Ongoing |
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**Title:** Total Colonic Manometry in the Evaluation and Management of Pediatric Functional Colonic Obstruction

**Principal Investigator:** MAJ Matthew J. Martin, MC

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**Department:** Surgery/General Surgery

**Facility:** MAMC

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**Associate Investigator(s):** CPT Scott R. Steele, MC; COL James M. Noel, Jr., MC; LTC David Wiechmann, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC

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**Keywords:** colonic manometry, pseudoobstruction, functional obstruction, motility

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**Start Date:**

7/24/2001

**Est. Completion Date:**

Indef

**Periodic Review:**

6/18/2002

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**Study Objective:** 1) Characterize basic patterns of normal and pathologic colonic motility on colonic manometry 2) Use total colonic manometry to diagnose the etiology of functional colonic obstruction 3) Establish a prospective clinical database of all patients referred for refractory functional obstruction that includes demographic data, colonic manometry results and interpretation, medical and surgical management, short and long term patient outcomes, and quality of life before and after intervention 4) Analyze manometry results, patient data, and treatment outcomes to increase the knowledge base of pediatric functional obstruction and design treatment strategies to maximize patient outcomes and quality of life.

**Technical Approach:** This will be a prospective study to collect and analyze a clinical database on all patients referred for refractory functional obstruction who undergo total colonic manometry. Any patient who is thought to be a candidate for surgery will have a surgeon's review of all data except manometry data. A written surgical opinion will be documented - the surgeon will be blinded to the patient's identification data at this point. A follow up surgical opinion will be obtained following manometric evaluation. Any change in the decision to proceed with surgery or any change in the planned procedure will be considered a positive impact. Chi-Square analysis will be used to determine if manometric data yields a change in surgical opinion. The surgeon will become unblinded when he meets the family after all data have been collected and opinions have been given.

It should be noted that this study will not change the way these patients are dealt with or evaluated in any fashion. Presently patients are evaluated with manometry and after a joint surgical and gastroenterologic evaluation a combined opinion on how to proceed is offered to the family. This will not change and will take place once the surgeon is unblinded. Thus this study evaluates the surgeon rather than the patient.

**Progress:** A total of 10 patients have been enrolled in the study, there have been no serious adverse events. Patient follow up continued during FY02. Data from this protocol has been presented at the Seattle Surgical Society Meeting 2001, The Gary P. Wratten Army Surgical Symposium 2002 and published in the Journal of Pediatric Surgery. An abstract is currently submitted to the American Pediatric Surgery Association.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/073

**Status:** Ongoing

**Title:** Ultrasound Imaging for Central Venous Catheter Placement in the Intensive Care Unit: Is Real-time Really Better? A Prospective Randomized Trial

**Principal Investigator:** MAJ Matthew J. Martin, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Michael Piesman, MC; CPT Scott R. Steele, MC; CPT Philip S. Mullenix, MC; LTC Leonard E. Deal, MC

**Keywords:** Ultrasound Imaging Central Venous Catheter Placement Real-time

**Start Date:**

5/28/2002

**Est. Completion Date:**

Dec 02

**Periodic Review:**

**Study Objective:** 1) To compare three methods of internal jugular central venous catheter placement in a prospective randomized fashion: anatomic landmarks only, ultrasound to evaluate the anatomy and mark the site, real-time ultrasound guidance. 2) Determine if internal jugular vein diameter is predictive of successful line placement and/or complications. 3) Analyze cost-effectiveness of using ultrasound for central line placement. 4) Analyze effect of patient factors such as age, body mass index, coagulopathy and prior same-site central lines on successful central venous catheter placement and complication rate. 5) Analyze effect of operator factors such as training level, department (medicine, surgery, emergency medicine, etc.) and prior experience on successful central venous catheter placement and complication rate

**Technical Approach:** In this study we will prospectively compare 3 different methods of internal jugular central venous catheter placement in 100 consecutive patients by random assignment: anatomic landmarks only, ultrasound to evaluate the anatomy and mark the site, real-time ultrasound guidance. We will examine data relating to patient factors including age, body mass index, previous central lines, and coagulopathy. We will also examine procedural data for each method to include number of needle passes, complications, success or failure of line placement, time of procedure, and internal jugular vein diameter. There will be no long term or outcome data studied. The 3 methods will then be compared for any statistically significant difference in ease of line placement, incidence of complications, and success rates. Data will also be analyzed by resident year group, experience level, and department of origin. Statistical analysis will be done using Student's t-test, analysis of variance, and chi-square or Fischer's exact test where appropriate.

**Progress:** This protocol is awaiting final approval following changes to the consent form to allow surrogate consent and changes to the power analysis.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/067 | <b>Status:</b> Terminated |
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**Title:** Acute Lung Injury Caused by Oleic Acid in the Rabbit (*Oryctolagus cuniculus*): Pathology, Free Radicals and Surfactant

**Principal Investigator:** CPT Rebecca M. McGuigan, MC

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| <b>Department:</b> Surgery/General Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT Philip S. Mullenix, MC; CPT Neil Stockmaster, MC; CPT David Ward, MC; LTC Kenneth S. Azarow, MC

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**Keywords:** Acute Lung Injury Oleic Acid Rabbit Pathology, Free Radicals and Surfactant

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**Start Date:**

**Est. Completion Date:**

**Periodic Review:**

jun 02

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**Study Objective:** The objective is to study oleic acid induced lung injury in rabbits and to compare this model to our established rat model. We hypothesize that the rabbits will be easier to ventilate and monitor in a controlled manner. We further hypothesize that free radicals will be produced and surfactant will be depleted. Finally, we hypothesize that melatonin will attenuate the injury created by oleic acid.

**Technical Approach:** General anesthesia will be induced using intramuscular (IM) injection of ketamine/xylazine and maintained using a continuous infusion of propofol. Angiocaths will be placed in the marginal vein of the ear and in the femoral artery by femoral cut-down. The animals will be intubated and placed on a mechanical ventilator. They will then be randomly assigned to experimental or control groups, each group consisting of 5 animals. All animals will receive hydroethidine (HE) injections and either oleic acid or albumin. There will be 3 groups as follows: Group A (Experimental, 5 animals): General anesthesia, intubation, intravenous HE and oleic acid injection. Mechanical ventilation for 6 hours. Group B (Experimental, 5 animals): Intravenous HE and oleic acid injection. Intravenous melatonin injection 3 hours following oleic acid. Monitor in oxygen chamber for total of 6 hours. Group C (Control, 5 animals): General anesthesia, intubation, intravenous HE and albumin injection. Mechanical ventilation for 6 hours. Each rabbit will receive HE solution. Each experimental animal will receive volume equal to 200mcL/kg oleic acid. Each control animal will receive an equal volume of 0.1% BSA. Oleic acid/albumin will be injected over a 15 minute period, 15 minutes following HE. Melatonin will be dissolved in ethanol, and then diluted in sodium chloride. Animals in group B will receive 10 mg/kg of melatonin 2 hours after oleic acid, while animals in groups A and C will receive an equal volume of saline. The animals will be ventilated and monitored for 6 hours. Arterial blood gases will be drawn from the femoral artery catheter at baseline (prior to oleic acid injection) and subsequently every hour.

**Progress:** This protocol was closed out due to technical difficulties which precluded the collection of meaningful data. No data analysis was performed.



### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/003                 | <b>Status:</b> Terminated |
| <b>Title:</b> Effect of Melatonin on Production of Superoxide in an Ex-vivo Placenta Ischemia-Reperfusion Model |  |                           |
| <b>Principal Investigator:</b> CPT Rebecca M. McGuigan, MC  |  |                           |
| <b>Department:</b> Surgery/General Surgery  |  | <b>Facility:</b> MAMC     |
| <b>Associate Investigator(s):</b> LTC Kenneth S. Azarow, MC   |  |                           |
| <b>Keywords:</b> free radical, superoxide, ischemia-reperfusion injury, melatonin, placenta model               |  |                           |
| <b>Start Date:</b><br>10/23/2001  | <b>Est. Completion Date:</b><br>Dec 01 | <b>Periodic Review:</b>   |

**Study Objective:** To show the presence of superoxide radicals in an ex-vivo placental ischemia-reperfusion model and the ability of melatonin to scavenge these radicals.

**Technical Approach:** This is a study of free radical production in an ex-vivo ischemia-reperfusion placental model. The goal is to measure the production of superoxide radicals in ischemia-reperfusion injury and the ability of melatonin to scavenge these radicals and/or prevent their production. We have recently shown that it is possible to measure the production of superoxide in an ischemia-reperfusion model in rats using a one time injection of hydroethidine (HE). Placental tissue from ten placentas will be reperfused with Hank's balanced salt solution and HE immediately following parturition. One cotyledon will be treated with melatonin and the other will not. Free radical production in both cotyledons will be measured using the conversion of hydroethidine to ethidium bromide. We expect that the cotyledon treated with melatonin will have less ethidium than the untreated cotyledon, therefore proving that melatonin is effective in scavenging free radicals and/or preventing their formation.

**Progress:** This study was terminated prior to its initiation at MAMC due to time constraints of the principal investigator.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/005 | <b>Status:</b> Ongoing |
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**Title:** Measurement Of Superoxide Radical In An ARDS Model In The Rat (Rattus Norvegicus)

**Principal Investigator:** CPT Rebecca M. McGuigan, MC

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| <b>Department:</b> Surgery/General Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Kenneth S. Azarow, MC; CPT Philip S. Mullenix, MC; CPT David Ward, MC

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**Keywords:** ARDS, free radicals, superoxide, nitrotyrosine, hydroethidine, lung, rat, animal model

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**Start Date:**

10/10/2001

**Est. Completion Date:**

Oct 02

**Periodic Review:**

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**Study Objective:** To demonstrate the presence of and measure the free radicals superoxide and peroxynitrite in an animal ARDS model using the conversion of hydroethidine to ethidium bromide and Western blot analysis for nitrotyrosine. This model will serve as a platform from which to evaluate potential modulating agents for the treatment and prevention of ARDS.

**Technical Approach:** A one time intravenous injection of hydroethidine followed by induction of ARDS by intravenous injection of oleic acid will be performed. Control rats will receive hydroethidine but will receive albumin injection in place of oleic acid. We will euthanize the animals after four or eight hours and measure the free radicals in the lung by measuring ethidium bromide fluorescence and the presence of nitrotyrosine by Western blot.

**Progress:** Finished animal portion, finishing bench component. Working on last 10% of this project. Abstract submitted. Will be done by end of CY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/120                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Steroidogenic Factor 1 (SF-1) in Human Breast Cancer Tissue   |  |                                      |
| <b>Principal Investigator:</b> CPT Rebecca M. McGuigan, MC  |  |                                      |
| <b>Department:</b> Surgery/General Surgery  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> LTC Kenneth S. Azarow, MC; Meera Ramayya, MD; Helmut Zarble, MD; CPT David Ward, MC |  |                                      |
| <b>Keywords:</b> Cancer: breast, aromatase, SF-1  |  |                                      |
| <b>Start Date:</b><br>7/24/2001   | <b>Est. Completion Date:</b><br>Sep 01 | <b>Periodic Review:</b><br>6/25/2002 |

**Study Objective:** This study will try to demonstrate the presence of mRNA and protein expression of Steroidogenic factor-1 (SF-1) and aromatase in estrogen receptor positive breast cancer cell lines and breast cancer tissue.

**Technical Approach:** This study will try to measure the presence of SF-1 and aromatase in breast cancer cell lines, normal breast tissue and breast cancer tissue. The following methods will be used: 1. RNA extraction and real time PCR; 2. Protein extraction and western blot; 3. Immunohistochemistry. In addition, cDNA microarrays will be used to determine if the expression of SF-1 alters the pattern of gene expression in breast tissue. Chi square test will be performed on the presence or absence of SF-1 with significance being a p value of less than 0.05.

**Progress:** A total of 6 patients have been enrolled during FY02. RNA samples from the tissues were tested for SF-1 by RT PCR and were negative.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/058 | <b>Status:</b> Ongoing |
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**Title:** Telomerase Activity in Metastatic Neuroblastoma: A Nude Mouse Model (mus musculus, nu/nu)

**Principal Investigator:** CPT Rebecca M. McGuigan, MC

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| <b>Department:</b> Surgery/General Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT James A. Sebesta, MC; LTC Kenneth S. Azarow, MC; CPT Jeffrey A. Vos, MC; CPT James Nunley, MC; M. J. DeHart, B.S.

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**Keywords:** telomerase, neuroblastoma, mouse,

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| <b>Start Date:</b> | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |
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10/11/2000

Nov 03

3/13/2002

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**Study Objective:** The objective is to evaluate the difference in telomerase activity between a primary neuroblastoma tumor and the subsequent foci of metastasis with the following objectives: 1) Telomerase activity in a metastatic foci of tumor is higher than that of the primary tumor. 2) Xenograft primary tumor will express morphologic differentiation as compared to the in vitro culture, and will therefore express a lower telomerase activity.

**Technical Approach:** Neuroblastoma tumor cells will be injected into immunocompromised mice. Once sufficient tumor growth has occurred, tumor tissue will be harvested and examined by DCI lab for telomerase activity.

**Progress:** Animal portion completed. Follow up bench/laboratory work ongoing.

### Detail Summary Sheet

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|---|------------------------------|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/080       | <b>Status:</b> Ongoing  |
| <b>Title:</b> The Fate and Therapeutic Impact of Exogenous Type II Pneumocytes in B6129SF2/J Mice                   |                              |                         |
| <b>Principal Investigator:</b> CPT Patrick M. McNutt, MS  |                              |                         |
| <b>Department:</b> <del>Surgery/General Surgery</del> Clinical Investigation  |                              | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> CPT Rebecca M. McGuigan, MC; LTC Kenneth S. Azarow, MC; MAJ Steven D. Mahlen, MC; |                              |                         |
| <b>Keywords:</b> acute respiratory distress syndrome mice pneumocytes   |                              |                         |
| <b>Start Date:</b>  | <b>Est. Completion Date:</b> | <b>Periodic Review:</b> |

**Study Objective:** Acute lung injury and acute respiratory distress syndrome (ARDS) make up a spectrum of disease with very high morbidity and mortality. Free radical production, damage to alveolar cells and surfactant depletion both cause and sustain ARDS. It is possible to reproduce ARDS in laboratory animals using an intravenous injection of oleic acid. The over all objective is to develop a post-onset therapy using type II pneumocytes to repopulate damaged alveoli and provide a short-term and long-term treatment. This study is a pilot to assess the ability of exogenously applied type II pneumocytes to engraft into host alveolar epithelium.

**Technical Approach:** This protocol will be performed in a series of experiments designed to measure the exogenous (allografted) pneumocytes in lung injury and to assess whether cultured or freshly harvested type-II pneumocytes are more efficient at engraftment. Lung tissue will be dissociated, purified for type II pneumocytes and either immediately administered or cultured, infected with an eGFP (enhanced green fluorescent protein) retroviral expression vector and co-injected with freshly-harvested cells. The survival, engraftment and morphology of the donor cells will be assayed at 1 and 5 days post-injection by colorimetric detection or fluorescence.

**Progress:** This protocol is approximately 25 percent completed. 28 percent of the authorized animals have completed the protocol, but data analysis is not yet possible.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/001 | <b>Status:</b> Ongoing |
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**Title:** Glycosylated Hemoglobin in Diabetics Undergoing General Surgery Procedures

**Principal Investigator:** CPT Philip S. Mullenix, MC

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**Department:** Surgery/General Surgery

**Facility:** MAMC

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**Associate Investigator(s):** CPT Christopher K. Sanborn, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC

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**Keywords:** diabetes, hemoglobin A1C, glycosylated hemoglobin, post-operative complications, clean-contaminated wounds, wound infection

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**Start Date:**  
10/24/2000

**Est. Completion Date:**  
Apr 01

**Periodic Review:**  
8/8/2002

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**Study Objective:** To determine if elevation of glycosylated hemoglobin is a predictor of post-operative complications in patients with diabetes mellitus.

**Technical Approach:** Subjects identified by the general surgery service and meeting inclusion criteria will have preoperative labs to include glycosylated hemoglobin, blood glucose, serum blood urea nitrogen, serum creatinine, and urinalysis. Oral hypoglycemics will be stopped the day prior to the scheduled procedure and not restarted until the patient restarts oral intake. For insulin dependent diabetics, ? the usual morning insulin dose will be given. On arrival, subjects will have their blood sugar checked and will be started on a solution of 5% dextrose. Demographics, the date of operation, use of prophylactic antibiotics, operative complications, postoperative complications, and other factors will be followed. The primary investigator will be blinded to the HbA1c data. At the end of the collection period, statistical analysis will be performed using chi-square. Wounds will be examined on postoperative day five and described as uncomplicated, seroma, or frankly infected. The seromas will be further subclassified as (1) gram stain negative, culture negative, (2) gram stain positive, culture negative, or (3) gram stain and culture positive.

**Progress:** No subjects enrolled within the last year. The new principal investigator, CPT Mullenix, plans to begin subject enrollment during FY03.

### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/074

**Status:** Ongoing

**Title:** Introduction of Telomerase into Type II Pneumocytes: Effect on Life Span and Surfactant Production

**Principal Investigator:**

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew J. Martin, MC; CPT Scott R. Steele, MC; CPT Todd M. Rossignol, MS; LTC Kenneth S. Azarow, MC; CPT Rebecca M. McGuigan, MC; CPT Patrick M. McNutt, MS

**Keywords:** telomerase, type II pneumocytes, surfactant, cell aging

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
7/24/2001

**Study Objective:** (1) Determine whether cells purchased from ACT will not have any significant telomerase activity or surfactant production prior to transfection with hTERT, (2) If ACT cells exhibit telomerase activity then they will not be used and we will attempt to culture and sustain a population of normal rat type II pneumocytes, (3) Transfect normal rat type II pneumocytes with a vector including the human telomerase catalytic subunit, (4) Assess telomerase activity in transfected cell population and control group, (5) Assess telomere length in transfected cell population and control group, (6) Assess pulmonary surfactant production in transfected cell population and control group, and (7) Stain transfected cell population and control group for B-galactosidase, a biological marker for cellular aging.

**Technical Approach:** Type II pneumocytes (CCL-149) will be purchased from ACT and grown to confluence. The cells will be extracted and telomerase activity will be assayed. If the cells exhibit a negative telomerase activity, then they will be used for the remainder of the study, if not, then a population of normal rat type II pneumocytes will be cultured from a rat lung. The appropriate cells will then be transfected with the nTERT cDNA gene. This will be accomplished using one of the procedures of transfection, either the bombardment techniques, Lipofectin or other. After transfection and growth of the cells to confluence, the cells will be assays again for Telomerase activity as above. Non transfected cells will be used as a control group. Telomere length will be determined. Pulmonary Surfactant production will be measured using either Western Analysis or another method as well as B-Galactosidase activity as a biological marker of cell aging.

**Progress:** Dr. Martin continues to try to introduce telomerase into the pneumocytes. This bench study remains ongoing.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 99/087      **Status:** Ongoing

**Title:** Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)

**Principal Investigator:** LTC Clifford A. Porter, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL William E. Eggebroten, MC; COL William C. Williard, III, MC; LTC Kenneth S. Azarow, MC; LTC Alan L. Beitler, MC; LTC David C. Elliott, MC; LTC David M. Watts, MC;

**Keywords:** Laparoscopic training, pig (Sus scrofa), esophageal surgery, gastric surgery

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Aug 02

**Periodic Review:**  
10/11/2000

**Study Objective:** To familiarize General Surgery residents, staff and invited surgeons from our community with techniques in the performance of advanced laparoscopic techniques. This training will include esophagus, stomach, biliary, small and large intestine, spleen, liver and retroperitoneal procedures. The training benefit will accrue to General Surgery residents, staff and invited surgeons by introducing these techniques or reinforcing earlier acquired skills in a controlled environment. Familiarity with these techniques will allow an increased margin of safety for patients decreased operative time, and minimizing of potential complications.

**Technical Approach:** Pigs will be maintained in an NPO status for 12 hours prior to the scheduled training procedures. An intramuscular tranquilizer will be used to aid in animal handling and preoperative management. General anesthesia will be induced with injectable agent and maintained by inhalational agent. Following anesthesia induction, pigs will be intubated endotracheally, will have an indwelling intravenous catheter placed in an ear vein for intraoperative fluid support, will have an orogastric tube inserted and connected to central suction for as-needed gastric decompression, and will be clipped and scrubbed as per aseptic surgery technique for the body regions of interest (e.g. abdomen, chest, etc.). Preoperative preparations will be conducted in the DCI animal surgery preparation and recovery room immediately adjacent to the DCI surgery. Following preoperative preparation, anesthetized animals will be transferred to either DCI surgery suite.

Five training sessions are scheduled for this training, they are: Advanced Laparoscopic Esophageal and Gastric Surgery, Advanced Laparoscopic Biliary Surgery, Advanced Laparoscopic Small and Large Intestinal and Rectal Surgery, Advanced Laparoscopic Splenectomy and Liver Surgery, and Advanced Laparoscopic Retroperitoneal Dissection and Lymph Node Dissection. Each session will be formalized into one day continuing medical education programs consisting of 1 hour of didactic lecture, 4 hours of hands-on procedural and/or instrumentation orientation using inanimate training models and non-living human or animal tissues, and 3 hours of live (anesthetized) animal laboratory for definitive procedural training. Each animal will be used for a single training session only, and will be euthanized at the end of the session without recovery from general anesthesia. Non-survival/training surgical procedures will be performed using clean (simulated aseptic) technique. Each training session will utilize up to four pigs.

**Progress:** This protocol was not used during FY02. LTC Robert Rush assumed protocol at the end of FY02.



### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/013                   | <b>Status:</b> Ongoing               |
| <b>Title:</b> Bariatric Surgery Effects on the Comorbidities of Obesity  |  |                                      |
| <b>Principal Investigator:</b> CPT Craig See, MC   |  |                                      |
| <b>Department:</b> Surgery/General Surgery   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> ; CPT James A. Sebesta, MC; LTC David M. Watts, MC; LTC Robert M. Rush, MC; LTC Clifford A. Porter, MC; LTC David C. Elliott, MC |  |                                      |
| <b>Keywords:</b> Resectional gastric bypass, Laparoscopic gastric bypass, gastric surgery, bariatric surgery, morbid obesity                                       |  |                                      |
| <b>Start Date:</b><br>11/27/2001   | <b>Est. Completion Date:</b><br>Mar 2006 | <b>Periodic Review:</b><br>12/2/2002 |

**Study Objective:** To determine and compare the effectiveness of resectional and laparoscopic gastric bypass in regards to reducing the comorbidities and mortality associated with morbid obesity.

**Technical Approach:** This study is a prospective observational study to analyze the effects of resectional and laparoscopic bypass on the morbidity and mortality of morbid obesity. All patients undergoing bariatric surgery at MAMC will be included in the study. A history, examination, and labs will be done preop, 3-6-and 12 months post-op. The variables and outcomes measured will include: weight, insulin/oral hyperglycemic requirement, fasting glucose, Hba1c, antilipid requirement, total cholesterol, LDL, HDL, triglycerides, antihypertensive requirement, blood pressure, sleep apnea screening questions, joint pain, panniculitis, hemoglobin, hematocrit, MCV, FE+, Ca+, vitamin B12, folate, prealbumin, and complications. Analysis of these outcomes of surgery will add significantly to the rationale behind bariatric surgery.

**Progress:** 64 subjects were prospectively enrolled during FY02 and 150 charts were retrospectively reviewed for a total of 214 subjects since study approval. There have been no adverse events associated with the protocol. One amendment was submitted and approved by the IRB during FY02 to add a quality of life questionnaire to the study. Subject enrollment continues.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/089 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Comparison of Harmonic Scalpel vs. Electrocautery Following Hemorrhoidectomy

**Principal Investigator:** CPT Scott R. Steele, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew J. Martin, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC

**Keywords:** Hemorrhoidectomy, harmonic scalpel, electrocautery

**Start Date:**

3/27/2001

**Est. Completion Date:**

Apr 02

**Periodic Review:**

4/23/2002

**Study Objective:** 1) Prospectively evaluate the post-operative pain and oral narcotic requirement after performing hemorrhoidectomy with a harmonic scalpel vs. electrocautery. 2) Evaluate the time to return to duty following hemorrhoidectomy using each procedure; 3) Determine differences in complication rates following hemorrhoidectomy after each procedure; 4) Evaluate the differences in blood loss and operative time following hemorrhoidectomy after each procedure.

**Technical Approach:** In this study we will compare the post-operative pain and narcotic use in 118 consecutive patients with symptomatic grade III or IV hemorrhoids when using the harmonic scalpel versus standard electrocautery while using maximal NSAID therapy. We will use a visual analogue scale for patients to quantify their pain pre-operatively and then on postoperative days 2 and 7. Post-operative narcotic requirements per 24 hours will similarly be recorded on post-operative days 2 and 7. We will call patients on postoperative day 28 to ensure no further complications. Data will be analyzed using a t-test.

**Progress:** Eighteen total patients have been enrolled with 11 since 1 Oct 02. Of those 11, 2 were disenrolled due to failure to turn in their data sheet. Patient enrollment and follow-up continuing during this next year.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/110                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Intra-operative Drain Use in Gynecomastia Patients Undergoing Subcutaneous Mastectomy             |  |                                      |
| <b>Principal Investigator:</b> CPT Scott R. Steele, MC  |  |                                      |
| <b>Department:</b> Surgery/General Surgery  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Matthew J. Martin, MC; LTC Kenneth S. Azarow, MC; LTC Ronald J. Place, MC |  |                                      |
| <b>Keywords:</b> gynecomastia, subcutaneous mastectomy, drain use, breast mass                                  |  |                                      |
| <b>Start Date:</b><br>6/26/2001   | <b>Est. Completion Date:</b><br>May 02 | <b>Periodic Review:</b><br>8/27/2002 |

**Study Objective:** Prospectively evaluate the complication rate associated with gynecomastia patients undergoing a subcutaneous mastectomy with and without intra-operative drain placement.

**Technical Approach:** Patients will be identified by the General Surgery Service. Any patient meeting the inclusion criteria for the study (as listed above) will be randomized prospectively to drain placement or no drain placement. Randomization will be performed by placing sealed envelopes in random order containing slips of paper with either “drain” or “no drain” inside in a three-ring binder. Randomization will occur in four consecutive groups of 8, with 4 “drains” and 4 “no drains” in each group. The General Surgery staff (RP) will have the binder. Envelopes will be taken consecutively with each new patient entered into the study and brought into the operating room at the time of operation sealed. Demographic data will be collected pre-operatively. A General Surgery resident and staff will then perform a standard subcutaneous mastectomy. Randomization will occur prior to skin closure. Additionally, patients will record post-operative narcotic use per 24 hours for the first ten days. Any patient requiring narcotic use past 10 days will be identified as having prolonged pain. All patients with a drain will follow-up in a standard clinic appointment on post-operative day 3, where the drain will be removed. Additionally all patients will follow-up in a standard clinic appointment on post-operative day 14. At the follow-up visits, we will assess the patient for possible complications via physical exam and by patient's history. The General Surgery staff will then keep the form, and a blinded investigator (KA) will make a follow-up phone call on post-operative day 28 to ensure no other complications occurred. Results will be analyzed using Chi-Square Analysis with significance level at  $p < 0.05$ .

**Progress:** The protocol began enrollment in Dec 01 and has continued to enroll 8 patients. Of those 3 had to be disenrolled secondary to lack of turning in data sheets. Subject enrollment and follow-up continues.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/020      **Status:** Ongoing

**Title:** Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis

**Principal Investigator:** CPT Amy L. Young, DO

**Department:** Surgery/General Surgery      **Facility:** MAMC

**Associate Investigator(s):** CPT James C. Nunley, MC; LTC Joseph P. Miller, MC; LTC Kenneth S. Azarow, MC; CPT Craig See, MC; CPT Jennifer E. Jorgenson, MC; LTC Gregory P. Fitzharris, MC; LTC Ronald J. Place, MC; LTC Alan L. Beitler, MC

**Keywords:** cumulative sum analysis, endotracheal intubation, airway assessment

**Start Date:**  
11/28/2000

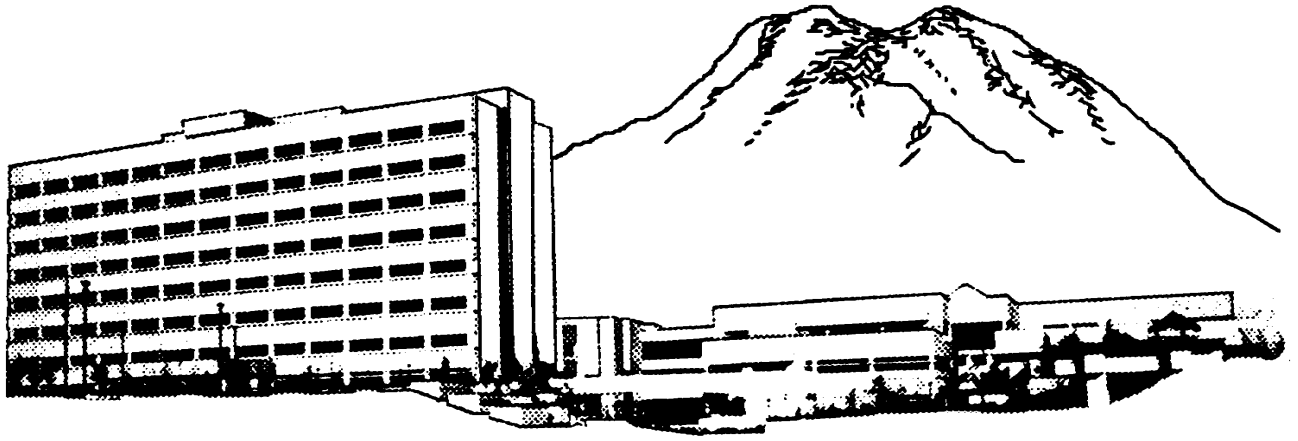
**Est. Completion Date:**  
Jul 02

**Periodic Review:**  
10/23/2001

**Study Objective:** (1) To evaluate individual and institutional learning curves for airway assessment by analyzing diagnostic accuracy as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, (2) To develop individual and institutional learning curves for the skill of endotracheal intubation as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, and (3) To evaluate a model (Cumulative sum analysis) for assessing the technical proficiency of surgical interns in the skills of airway assessment and endotracheal intubation.

**Technical Approach:** Surgical interns will receive standardized training on airway anatomy and assessment coupled with a practical session on intubation in ATLS models. These house officers will then perform airway assessments and endotracheal intubations on surgical patients who are 18 years or older, ASA class I or II, and who do not require rapid sequence intubation. Each attempt will be supervised and scored by a staff anesthesiologist or CRNA using a standardized data sheet. A successful assessment will be one where the airway classification matches the supervising staff's determination. A successful intubation will be insertion of an endotracheal tube within 30 seconds of laryngoscopy initiation, documented by end tidal CO<sub>2</sub>. If an attempt is unsuccessful, the process may be repeated. Each consecutive attempt will be recorded separately. A data sheet will be filled out and a new score assigned for each attempt, even when there are multiple attempts on a single patient. Supervising staff will determine if and when they need to step in and intubate the patients themselves. Data sheets will be turned in to the principal investigator, who will calculate CUSUM values and plot learning curves. Data will be monitored during the rotation. At the completion of the 4-week experience, these results will be shared with the interns and staff. After an entire class of interns has completed the rotation, the results will be submitted for publication and presentation.

**Progress:** Eight healthcare providers participated in this study during FY02, for a total of 11 overall. Learning curve for intubation appears to be 19. Paper submitted to Society of University Surgeons. Addendum for endoscopy to begin this FY.



## **Detail Summary Sheets**

# **Ophthalmology Service, Department of Surgery**

## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 200/117

**Status:** Ongoing

**Title:** A Pilot Study on the Use of Laser Assisted In-Situ Keratomileusis (LASIK) versus Photorefractive Keratectomy (PRK) in Active Duty U.S. Army Personnel for the Correction of Myopia and Astigmatism

**Principal Investigator:** COL Vernon C. Parmley, MC

**Department:** Surgery/Ophthalmology Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Keith F. Dahlhauser, MC; MAJ Steven M. Brady, MC; MAJ Robert B. Carroll, MC; CPT Clifton S. Otto, MC; CPT William Lim, MC

**Keywords:** myopia, astigmatism, laser assisted in-situ keratomileusis (LASIK), photorefractive keratectomy (PRK), flying spot, active tracking, military readiness, military specific

**Start Date:**

8/22/2000

**Est. Completion Date:**

Dec 03

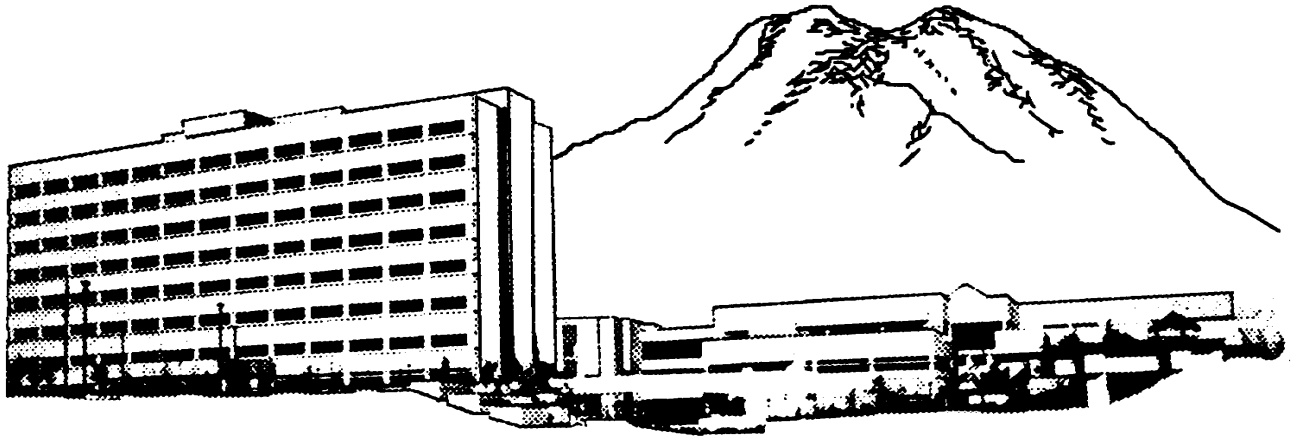
**Periodic Review:**

6/7/2002

**Study Objective:** The purpose of this study is to compare laser assisted in-situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) using the Summit® autonomous excimer laser system and the Bausch and Lomb Hansatome® keratome as surgical methods for treating myopia and astigmatism in active duty soldiers.

**Technical Approach:** Approximately five hundred subjects who meet the inclusion criteria and who are active duty Army personnel between the ages of 21-55 with non-flying duties will be invited to participate in this study. The Argon fluoride excimer laser (193nm wave length) will be used to reduce the myopia and astigmatism of spectacle or contact lens dependent soldiers according to standard nomograms build into the laser controlling software of the excimer. Central ablation diameter will be 6.5 mm. Preoperative Assessments: Clinical examination will include past ocular and medical history, eye surgery or trauma, current medications, possible allergies, and a review of previous examinations and refractions. Hard contact lenses must be removed four weeks prior to the examination, and soft contact lenses must be removed one week prior to evaluation. Pupil size, uncorrected and best corrected visual acuity, manifest and cycloplegic refraction, keratometry and corneal topography, intraocular pressure, slit lamp biomicroscopy, central pachymetry, dilated ophthalmoscopy, and glare contrast sensitivity will be completed during the preoperative assessment and at the third month and one year examination. Subjects must be available for one year follow-up. If the volunteer states his/her desire to participate in the study, the consent process will be completed and a surgical date scheduled. On the day of surgery, each subject will be randomized (computer generated randomization) to undergo either bilateral sequential LASIK or PRK. All postoperative examinations will be performed at Madigan Army Medical Center. The subject will be examined on day 1, day 3, day 7, 1 month, 3 months, 6 months and 1 year. At the one-month, three-month and one year evaluations, subjects will complete a questionnaire that subjectively assesses quality of vision and satisfaction with the procedure, as well as their subjective assessment of their ability to perform in their MOS. At the one-week evaluation, subjects will also indicate number of days after the procedure before they could return to full duty. If they have not returned to full duty by the one-week evaluation, this will be noted with a comment to ask again at the one-month evaluation if the patient has returned to full duty. The questionnaire used in this study is patterned after the functional vision test used in prospective evaluation of radial keratotomies study and the VF-14 visual function test developed for assessing visual performance in patients with cataracts.

**Progress:** The laser was delivered to MAMC on 30 September 2002. It will be assembled and calibrated this week. Partial training will take place on 10 and 11 October 2002. Investigators are still in the process of hiring technicians, who will need to be trained. It is hoped that the study will be able to treat its first enrolled patients within the next 4 to 6 weeks. This represents definite progress!



## **Detail Summary Sheets**

### **Orthopedics Service, Department of Surgery**

### Detail Summary Sheet

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|------------------------|-----------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 96/086 | <b>Status:</b> Completed |
|------------------------|-----------------------|--------------------------|

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**Title:** A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough

**Principal Investigator:** LTC Edward D. Arrington, MC

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|---|-----------------------|
| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** Hollis Potter, M.D.; CPT Roger W. Dougherty, SP; COL Patrick St Pierre, MC

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**Keywords:** Rotator cuff, cortical bone, cancellous trough,

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|---------------------------------|--|---------------------------------------|
| <b>Start Date:</b><br>3/15/1996 | <b>Est. Completion Date:</b><br>Apr 99 | <b>Periodic Review:</b><br>10/23/2001 |
|---------------------------------|--|---------------------------------------|

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**Study Objective:** To determine if tendon repair to a cancellous trough is necessary for rotator cuff repair in humans.

**Technical Approach:** Forty patients with proven rotator cuff tears will be randomized to two surgical groups. Group A will have their rotator cuff tendon repaired to the greater tuberosity after a trough is made in the greater tuberosity of the humerus. Group B will have their rotator cuff repaired to the cortical bone of the greater tuberosity of the humerus without the creation of a trough. A thorough debridement of soft tissue to include bursa and scar will be performed in both groups. Postoperative treatment will be the same for each group. Clinical evaluations and physical exams to include range-of-motion, shoulder impingement signs and tenderness will be performed at one, six, twelve and twenty-four month follow-ups by the physical therapist department. The modified Hospital for Special Surgery (HSS) Score as well as an analog pain, function, and satisfaction score will be used for clinical evaluation. A significant difference in the assessment of strength scores would indicate superiority of one method over the other. MRI evaluations will be performed at six, twelve and twenty-four months. The MRI will be evaluated by an MRI radiologist at the HSS in New York City, New York, who will be blinded to the method of treatment for each patient. Criteria for success by MRI has been established by a recent study performed at the HSS by the radiologist and the principle investigator.

**Progress:** No patients have been enrolled during FY 02. Final clinical and radiographic evaluation of study participants has been completed, and an abstract is pending from the original principal investigator, COL Patrick St. Pierre, MC.



### Detail Summary Sheet

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|--|--|--------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 201/016                 | <b>Status:</b> Completed |
| <b>Title:</b> Biomechanical Comparison of a New Modified Mason-Allen Suture Anchor Technique with Traditional Methods in Rotator Cuff Repair   |  |                          |
| <b>Principal Investigator:</b> CPT Brendon R. Connolly, MC   |  |                          |
| <b>Department:</b> Surgery/Orthopedic Surgery  | <b>Facility:</b> MAMC                  |                          |
| <b>Associate Investigator(s):</b> COL Patrick St Pierre, MC; CPT Kurtis L. Kowalski, MC  |  |                          |
| <b>Keywords:</b> suture anchors, rotator cuff repair, modified Mason-Allen   |  |                          |
| <b>Start Date:</b><br>10/24/2000   | <b>Est. Completion Date:</b><br>Sep 00 | <b>Periodic Review:</b>  |
| <p><b>Study Objective:</b> Collect information regarding the strength and biomechanical characteristics of new absorbable suture anchors combined with a modification of a previously described suture technique for use in repairs of the rotator cuff. Compare these results with traditional methods of suturing and rotator cuff reattachment as well as currently available non-absorbable suture anchors.</p> <p><b>Technical Approach:</b> Thirty rotator cuff/proximal humerus specimens will be harvested from fresh-frozen human cadavers. The rotator cuff will be divided at its insertion on the humeral head. The rotator cuff will be repaired using 6 methods - new modified Mason-Allen suture anchor technique with either the Mitek Panalok RC, the Arthrex Biocorkscrew, or the Fastin RC; the arthroscopic double-mattress technique using the Fastin RC and the Arthrex Biocorkscrew; and the traditional transosseous technique with a horizontal mattress suture. Five examples of each method will be tested and the results averaged within each group. Number 2 Ethibond suture will be used for every repair. The rotator cuff and humerus will then be attached in an identical and reproducible manner to specialized bone and tendon clamps. Biomechanical testing will be performed with the Instron device. A cyclic pre-load of five newtons will be applied for five cycles (7). Each specimen will then be tested to tensile failure at a uniform rate of displacement. The resulting load-deformation curve will then be used to calculate the energy to failure, maximum load to failure, and peak stiffness. The mode of failure (anchor pullout, eyelet breakage, suture breakage, knot failure, or tendon failure) will also be documented. Data will be evaluated using a one-way ANOVA to determine differences between groups. Also, the Student's paired t-test will be used to determine the significance of the differences between the types of repair with respect to all the matched outcome variables.</p> <p><b>Progress:</b> All work on this protocol has been completed and a powerpoint presentation of the study findings is available.</p> |  |                          |

### Detail Summary Sheet

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|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/128 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** A Prospective, Multicenter, Open-Label Study to Evaluate the Safety and Efficacy of Apligraf in the Treatment of Diabetic (Primarily Neuropathic) Foot Ulcers That Have Not Adequately Responded to Standard Therapy (Protocol #CGSO769B US08)

**Principal Investigator:** Vickie R. Driver, DPM

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|---|-----------------------|
| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
|---|-----------------------|

**Associate Investigator(s):** Charles A. Andersen, M.D.; CPT Troy N. Morton, MC

**Keywords:** DFU-Diabetic foot ulcer, QOL-Quality of Life, TU, Target ulcer, NCR-No carbon required, CS&E-Clinical Safety and Epidemiology

**Start Date:**  
8/28/2001

**Est. Completion Date:**  
Jan 03

**Periodic Review:**

**Study Objective:** Primary: Evaluate the safety and efficacy of Apligraf in patients with diabetic (primarily neuropathic) foot ulcers that have not adequately responded to standard therapy and to determine the time (in days) to complete healing of the target wound. Complete wound healing is defined as full epithelization of the wound with the absence of drainage.

**Technical Approach:** This will be an open-label, study in approximately 100 patients with diabetic (primarily neuropathic) foot ulcers at up to 20 centers. Study duration is 12 weeks with 3 months follow-up. Patients with ulcers that appear to be healing spontaneously during the screening period (>30% reduction in area within 7 days prior to application of Apligraf) will not proceed to the treatment period. The remaining patients with ulcers that are thus defined as being hard to heal may enter the treatment period; however, patients with clinically infected ulcers must not be allowed in the study.

The screening period will occur within 1 week prior to the Treatment Period. The wound will be surgically debrided and dressed. The dressing will stay in place for 1 week. Patients will be instructed on off-loading. The Investigator will order Apligraf and patients will return the following week for the initial application of Apligraf. During the treatment period, Day 0 up to Week 12, the wound will be evaluated prior to the application of Apligraf. Patients who still satisfy the inclusion/exclusion criteria will have Apligraf applied at Day 0. A second application is permitted. Safety and efficacy evaluations will be performed weekly. Efficacy will be assessed by clinical observations at weekly visits. Photographs will be obtained at baseline and at each visit thereafter for the duration of the study. Wound tracings will be performed at selected timepoints. Safety will be assessed by clinical observation including signs and symptoms of infection. The study completion will be defined as the time of complete wound healing or 12 weeks after initial application of Apligraf. If healing is achieved prior to Week 12, the patient will proceed immediately to the week 12 evaluations and enter the follow-up period. All patients will have three monthly follow-up visits after Week 12 (or documented healing). In addition, patients who have target ulcers that have healed by or at 12 weeks will be evaluated weekly for two weeks following documented healing. The primary efficacy variable will be time to complete wound healing, defined as full epithelialization of the wound with the absence of drainage. Secondary efficacy variables are the incidence of 100% wound healing at Week 12 and for patients whose ulcer healed, the next two weekly assessments will evaluate whether the healing was sustained for two consecutive visits. The follow-up period starts at the visit the physician indicates the target ulcer is 100% healed.

**Progress:** A total of 5 patients enrolled in this study at MAMC. All 5 patients received study treatment, and completed entire study procedures during FY02.

## Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/081                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Prospective, Randomized, Comparative, Parallel Study of Hyalofill Wound Dressing in the Management of Indolent Diabetic Foot Ulcers   |  |                                      |
| <b>Principal Investigator:</b> Vickie R. Driver, DPM  |  |                                      |
| <b>Department:</b> Surgery/Orthopedic Surgery   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> Charles A. Andersen, M.D.; LTC Jeffrey P. Zimmerman, MS; CPT Troy N. Morton, MC; Mary Anne Landowski, RN; James Hsing-Hsi. Lee, DPM; Eric J. Heit, DPM  |  |                                      |
| <b>Keywords:</b> diabetic foot, neuropathic ulcer, indolent, debridement  |  |                                      |
| <b>Start Date:</b><br>2/27/2001   | <b>Est. Completion Date:</b><br>Apr 03 | <b>Periodic Review:</b><br>3/26/2002 |
| <p><b>Study Objective:</b> The primary objectives is to compare the proportion of ulcers completely healed by the Hyalofillä protocol of care to the standard protocol of care to the management of indolent diabetic ulcers.</p> <p><b>Technical Approach:</b> This is a prospective, stratified, randomized, comparative, parallel group, multi-center clinical trial comparing the number of ulcers completely healed by the Hyalofill™ protocol of wound care to the standard protocol of wound care, as outlined by ConvaTec, in diabetic patients with an indolent diabetic foot ulcer with adequate arterial perfusion, for wound healing to the affected limb. A total of 200 patients will be enrolled with about 10 patients enrolled at MAMC. Patients will be stratified by Wagner Grade and location prior to randomization and will be assigned to either a wound care protocol of Hyalofillä or the standard protocol of wound care, as outlined by ConvaTec. Individual study participation is 20 weeks or to complete healing (100% re-epithelialized), whichever occurs first. ConvaTec defines standard of care for the purposes of this protocol as: (1) Sharp debridement to remove necrotic tissue, (2) If the wound is dry, DuoDERM Gel will be used. If the wound requires exudate management, Kaltostat wound dressings will be used, (3) Either of these two products will receive Allevynä Non-Adherent as a cover dressing, (4) The foot ulcer will then be appropriately supported with either Aircast (plantar) or accomodative footwear (non-plantar), depending upon the ulcer location. The Hyalofill protocol care group is defined as: (1) Sharp debridement to remove necrotic tissue, (2) If the wound is dry, Hyalofill will be pre-moistened with normal saline and placed directly on the wound, (3) If deemed necessary by the Investigator, DuoDERM Gel may be used and placed directly on top of the Hyalofill™ dressing, (4) If the wound requires exudate management, Hyalofill™ will be placed directly on the wound, (5) If deemed necessary by the Investigator, Kalostat dressings may be used and placed directly on top of the Hyalofill™ dressing. Patients will be seen weekly until 20 weeks or wound healing whichever occurs first. At each weekly assess-ment, the wound will be debrided (if necessary), the investigator will assess the ulcer, and a peri-ulcer description will be performed. At Weeks 4, 8, 12 and 16, an acetate tracing and photograph of the ulcer will be obtained. At week 20 or healing, a blood sample will be obtained to assess metabolic control, an acetate tracing and photograph of the ulcer will be performed and both the ulcer and pre-ulcer descriptions will be done. Cost Effectiveness will be calculated using Mean time to healing, Percentage of ulcers completely healed in 20 weeks, Cost associated with dressing changes (e.g., labor, dressing supplies), and Complications (e.g., infection, in-patient hospital stay and procedures related to the study ulcer).</p> <p><b>Progress:</b> A total of 31 patients were enrolled, 12 of these patients have been enrolled since 01 October 2001. 8 patients were screen failures. 23 patients received study treatment, 2 patients died while participating in this study however these deaths were considered unrelated to study participation. 21 patients remain in follow-up. This study is closed to enrollment.</p> |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/091 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Prospective, Randomized, Stratified, Parallel Group, Comparison Study of the Healing Rate of Chronic Neuropathic Ulcers Treated with Hyalofill VS Regranex

**Principal Investigator:** Vickie R. Driver, DPM

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Jeffrey P. Zimmerman, MS; Charles A. Andersen, M.D.; John Lord, DPM; Tanya Thoms, DPM

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**Keywords:** hyaluronic acid, regranex, becaplermin neuropathic ulcer growth factor

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**Start Date:**

6/25/2002

**Est. Completion Date:**

Mar 02

**Periodic Review:**

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**Study Objective:** Compare the treatment time required for complete wound repair of two wound healing products currently available for diabetic wound care (Hyalofill VS Regranex)

**Technical Approach:** This is a prospective, randomized, stratified, comparative, parallel group, one center clinic trial, comparing the time to wound closure of indolent ulcers healed by Hyalofill protocol of wound care to protocol of Regranex gel. Madigan Army Medical Center will enroll 55 total patients. Patient will be stratified according to ulcer location to randomization and will be assigned to either Regranex or Hyalofil protocol. All subjects will participate in the 20 week study or to complete 100% re-epithelization, whichever occurs first. The objective of this study is to compare the mean time to closure of ulcers, Time to wound closure will be measured in weekly increments.

**Progress:** This study has not yet begun here at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/071                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy in the Treatment and Blinded Evaluation of Venous Stasis Ulcers (Protocol VAC2001-02) |  |                         |
| <b>Principal Investigator:</b> Vickie R. Driver, DPM  |  |                         |
| <b>Department:</b> Surgery/Orthopedic Surgery   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> Charles A. Andersen, M.D.; Mary Anne Landowski, RN; James Hsing-Hsi. Lee, DPM; John Lord, DPM; Tanya Thoms, DPM                                 |  |                         |
| <b>Keywords:</b> vacuum assisted closure therapy venous stasis ulcers ankle brachial index  |  |                         |
| <b>Start Date:</b><br>5/28/2002   | <b>Est. Completion Date:</b><br>Jul 04 | <b>Periodic Review:</b> |

**Study Objective:** The primary objectives are the incidence of wound closure, accelerated ulcer closure and reduction in ulcer area over time. The secondary objectives are the reduction in complications, pain reduction, improved quality of life and reduction in average total cost of care.

**Technical Approach:** This study will be looking at approximately 10 males or females, 18 years of age or older, that have venous stasis ulcers >30 days duration and < 100 CM<sup>2</sup> in area. To be eligible for this study a valid, signed informed consent must be obtained for each patient who meets all inclusion/exclusion criteria. Questions will be answered by the primary investigator or a study coordinator. Relevant medical and surgical history will be taken; physical exam, calculation of ABI/Doppler Arterial Waveforms will be determined for each patient; vascular studies with a positive venous reflux test will be performed; concomitant medications recorded; blood will be drawn for laboratory tests and Quality of Life questionnaire completed; digital photography will be performed; bi-layer tracing of the wound will be measured; granulation tissue formation will be categorically estimated in % and recorded; patient will complete the wound pain assessment using the VAS about one-half hour prior and one-half hour after the wound dressing changes. Interim dressing changes will be documented as well as any serious adverse effects. The purpose of this study is to compare negative pressure therapy using the V.A.C. and treatment according to institutional protocols consistent with standard of care. KCI is completing the data analysis.

**Progress:** This study has not yet begun at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/086 | <b>Status:</b> Ongoing |
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**Title:** A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Diabetic Foot Ulcers (Protocol VAC2001-08)

**Principal Investigator:** Vickie R. Driver, DPM

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** Charles A. Andersen, M.D.; Mary Anne Landowski, RN; John Lord, DPM; Tanya Thoms, DPM

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**Keywords:** vacuum assisted closure diabetic foot ulcer ankle brachial index

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**Start Date:**

6/25/2002

**Est. Completion Date:**

Aug 05

**Periodic Review:**

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**Study Objective:** The primary objectives are to determine the incidence of complete ulcer closure, accelerated ulcer closure or facilitation of surgical closure, and change in ulcer area. The secondary objectives are to determine the reduction in complications, including amputations, quality of life, and average total cost of care.

**Technical Approach:** This study will be looking at approximately 18 male or female patients 18 years of age or older that have diabetic foot ulcers > 2cm<sup>2</sup> in area after debridement. To be eligible for this study a valid signed informed consent form must be obtained for each patient and each patient must meet all inclusion/exclusion criteria. Patient questions will be answered by the primary investigator or a study coordinator. A copy of the informed consent will also be given to the patient for their keeping. Visit #1-Eligible patients will be given a physical exam, a relevant medical and surgical history will be taken, concomitant medications will be listed, blood drawn for laboratory tests and the patient will be given a Quality of Life Questionnaire to complete. Visit #2, the patient will be randomized and given their first treatment. At subsequent visits the study group patients will have medical and medication histories updated, digital photographs will be taken of the wound, measurements taken, dressing applied and instructions on continued care given. The control group will receive standard of care treatment. All patients will receive off-loading therapy preventatively and therapeutically as indicated. Off-loading therapy is used to keep pressure away from the wound area by means of the use of a special shoe, boot, cane, or, in some cases, a wheelchair. No patient will remain in the study for longer than 12 months (total duration). The wound will be examined for recurrence or determination of ulcer status. The purpose of this study is to compare the incidence of wound closure, the facilitation of ulcer closure and the reduction in ulcer area in the V.A.C group vs. the control therapy group. Secondary aims include comparisons of foot salvage at one year post-treatment initiation. KCI is completing the data analysis.

**Progress:** This study has not yet begun at MAMC.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/115                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Amputation Wounds of the Diabetic Foot, Protocol No. VAC2001-07 |  |                         |
| <b>Principal Investigator:</b> Vickie R. Driver, DPM  |  |                         |
| <b>Department:</b> Surgery/Orthopedic Surgery   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> Charles A. Andersen, M.D.; Mary Anne Landowski, RN  |  |                         |
| <b>Keywords:</b> Vacuum Assisted Closure Therapy Amputation Wounds Diabetic Foot  |  |                         |
| <b>Start Date:</b><br>9/24/2002   | <b>Est. Completion Date:</b><br>Sep 05 | <b>Periodic Review:</b> |

**Study Objective:** The primary objectives are to determine the incidence of complete wound closure, accelerated wound closure or facilitation of surgical closure, and change in wound area over time. The secondary objectives are to determine the incidence of foot salvage, as defined by retention of transmetatarsal amputation with no further revisions at end of study, incidence of complications, quality of life, and average total cost of care

**Technical Approach:** This study will be looking at approximately 8-10 male and female patients 18 years of age or older that have amputation wounds of the diabetic foot. To be eligible for this study a valid signed informed consent form must be obtained for each patient and each patient must meet all inclusion/exclusion criteria. Patient questions will be answered by the primary investigator or a study coordinator. A copy of the informed consent will also be given to the patient for their keeping. Visit #1-Eligible patients will be given a physical exam, a relevant medical and surgical history will be taken, concomitant medications will be listed, blood drawn for laboratory tests and the patient will be given a Quality of Life Questionnaire to complete. Visit #2, the patient will be randomized and given their first treatment. At subsequent visits the study group patients will have medical and medication histories updated, digital photographs will be taken of the wound, measurements taken, dressing applied and instructions on continued care given. The control group will receive standard of care treatment. All patients will receive off-loading therapy preventatively and therapeutically as indicated. Off-loading therapy is used to keep pressure away from the wound area by means of the use of a special shoe, boot, cane, or, in some cases, a wheelchair. No patient will remain in the study for longer than 12 months (total duration). The wound will be examined for recurrence or determination of ulcer status. The purpose of this study is to compare the incidence of complete wound closure, the facilitation of ulcer closure and the reduction in ulcer area in the V.A.C group vs. the control therapy group. KCI is completing the data analysis.

**Progress:** This study has not yet begun at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/098      **Status:** Completed

**Title:** Linezolid IV or PO Compared to Unasyn® IV or Augmentin® PO for the Treatment of Patients with Diabetic Foot Infections-A Randomized, Open-label Phase IV Clinical Trial

**Principal Investigator:** Vickie R. Driver, DPM

**Department:** Surgery/Orthopedic Surgery      **Facility:** MAMC

**Associate Investigator(s):** Charles A. Andersen, M.D.; LTC Jeffrey P. Zimmerman, MS; Mary Anne Landowski, RN; CPT Troy N. Morton, MC; CPT Alec C. Beekley, MC; Eric J. Heit, DPM; James Hsing-Hsi. Lee, DPM

**Keywords:** ECG -12-lead electrocardiogram, HAP- Hospital-acquired or nosocomial pneumonia

**Start Date:**  
5/22/2001

**Est. Completion Date:**  
May 03

**Periodic Review:**  
5/28/2002

**Study Objective:** Primary Objective: To assess the clinical effectiveness, safety, and tolerance of intravenously and orally administered Linezolid when compared with Unasyn® IV and Augmentin® PO in treating diabetic foot infections. Selected Additional antibiotic agents may be added to each treatment arm for specific indications. Secondary Objectives: To assess the microbiological efficacy (i.e. bacteriological eradication rate) of each treatment arm, to compare the clinical outcome of selected subsets of enrolled subjects, e.g., those initially treated as outpatients vs. inpatients; those treated with oral vs. intravenous agents; those with or without osteomyelitis, and to assess predictive value of the probe to bone test in the diagnosis of osteomyelitis.

**Technical Approach:** This randomized, open label, comparator-controlled study will compare the clinical efficacy, microbiological efficacy, safety, and tolerability of the two regimes in the treatment of diabetic foot infections: Linezolid IV or PO (600 mg every 12 hours). All enrolled patients can start therapy with either IV or PO Linezolid. The investigator can switch from IV to PO Linezolid at anytime during the course of Patient therapy. Outpatients will start with PO Linezolid only. Unasyn IV (3g every 6 hours) or Augmentin PO (500 mg every 8 hours) for hospitalized patients. Patients receiving Unasyn can switch to Augmentin PO at the investigators' discretion. For outpatient settings, patients can be randomized to Augmentin PO (500 mg every 8 hours). If the patient is assigned to the Unasyn/Augmentin treatment group and they are MRSA positive, they will receive an IV treatment with Vancomycin.

Patients enrolled will be randomized to one of these two treatment arms. The intended treatment duration is 14 days for both treatment arms to include a screening visit, Day 7, Day 14, Day 21 and End of Treatment visit to evaluate response. If osteomyelitis, infection in the bone, is present the investigator may treat the patient with the study regimen up to 28 days. Upon switching to oral medication a clinical observation will be made (including wound description and vital signs). A final Follow-up Visit will occur after the End of Treatment Visit between day 21-28 to assess the wound and evaluate clinical response.

**Progress:** This study was reported as completed by the principal investigator, Apr 02, with a final close-out site visit by the study sponsor, Sep 02. A total of 18 patients were screened and randomized. 17 subject completed the study. One subject did not complete the study due to early termination by PI. Two MAMC adverse events had been reported; (1) ascending cellulitis and (2) partial amputation. Both events were deemed not related to study participation by the principal investigator.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/002

**Status:** Ongoing

**Title:** A Double-blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Single-dose, Subcutaneous (SC) Darbepoetin Alfa in Subjects Undergoing Preoperative Autologous Blood Donation (PAD) Before Elective Knee or Hip Surgery, Protocol Darbepoetin Alfa 20010117

**Principal Investigator:** MAJ James A. Hall, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Doug A. Vermillion, MC; Christopher J. LeBrun, M.D.

**Keywords:** Darbepoetin Alfa Autologous Blood Surgery.

**Start Date:**  
10/23/2001

**Est. Completion Date:**  
Oct 02

**Periodic Review:**  
10/22/2002

**Study Objective:** Primary: To evaluate whether a single, subcutaneous dose of darbepoetin alfa (dose: 6.5 µg/kg) reduces allogeneic blood transfusions compared to placebo in subjects enrolled in a PAD program. Secondary: To evaluate the safety profile of darbepoetin alfa compared to placebo in subjects enrolled in a PAD program.

**Technical Approach:** This Darbepoetin alfa study is a Phase III, double-blind, randomized, placebo controlled study to evaluate whether a single SC dose of Darbepoetin alfa reduces allogeneic blood transfusion compared to placebo in subjects enrolled in a program for preoperative autologous blood donation (PAD), and who will undergo elective revision total hip replacement or bilateral knee replacement surgery. The primary endpoint will be the proportion of subjects receiving an allogeneic blood transfusion in the intra- and postoperative period. Secondary endpoints will include total units of allogeneic blood transfused in this period; total units of autologous blood donated; total units of autologous blood transfused in the intra- and postoperative period; and the nature, frequency, severity, and relationship to treatment of all adverse events. Approximately 6 subjects will be enrolled at MAMC. 240 subjects will be enrolled overall in approximately 40 study centers, 120 randomized to receive darbepoetin alfa, and 120 to receive placebo, stratified by center, surgical procedure, and baseline hemoglobin level. Subject screening will take place between days -42 to -22 before surgery and following documentation of informed consent. Study assessments, a single dose of Darbepoetin alfa (6.5 µg/kg) or placebo will be administered, and PAD will begin at day -24 to -21. Study assessments and PAD will proceed on days -14 (± 2) and -5 (± 2). On Day of surgery (Day 0), study assessments will take place prior to anesthesia or surgery procedures. On days 5 (± 3) and 14 (± 3) study assessments will be made and on day 40 (±5), end of study evaluations will be completed. Adverse events and their relationship to study drug will be recorded throughout. Data will be summarized with descriptive analysis, and analysis of variance will be performed for treatment groups and differences between treatment groups. From time of start of enrollment to completion of study activities by the final enrolled patients will be a period of approximately one year.

**Progress:** No patients have enrolled in this study at MAMC to date. An amendment to this protocol was approved, Aug 02, allowing consent to pre-screen for Hgb due to high screen failure.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 200/065 | <b>Status:</b> Ongoing |
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**Title:** Study of the Treatment of Articular Repair (STAR): A Prospective, Longitudinal Within Patient Evaluation of the Effectiveness (Durability) of Carticel (autologous cultured chondrocytes) Compared to Non-Carticel Surgical Treatment for Articular Cartilage Defects of the Knee

**Principal Investigator:** MAJ James A. Hall, MC

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Doug A. Vermillion, MC; COL Patrick St Pierre, MC

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**Keywords:** Articular repair, Articular Cartilage Defects, autologous cultured chondrocytes, Carticel implantation

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**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Jun 06

**Periodic Review:**  
4/23/2002

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**Study Objective:** To compare the effectiveness (durability) of Carticel autologous chondrocyte implantation in patients who have had an inadequate response to a prior non-Carticel surgical cartilage repair procedure (including debridement, microfracture, drilling, abrasion arthroplasty or other surgical treatment) within the previous 3 years for significant articular cartilage defects of the femoral condyle.

**Technical Approach:** This study will be a longitudinal, prospective, multicenter, within patient evaluation of 100 patients with articular cartilage defects of the knee who have had inadequate response to a prior non-Carticel surgical treatment. Patients who had an inadequate response to a prior non-Carticel surgical treatment will be implanted with Carticel (autologous cultured chondrocytes). the overall condition of the knee will be evaluated Using Modified Cincinnati Knee Rating System at baseline and every 6 months postoperatively. The SF-36 health survey will be used to assess global health status at baseline and follow-up visits. The primary endpoint of the study will be time to treatment failure, and will be compared via chart review of consented patients to the durability of past treatments.

**Progress:** A total of 5 patients enrolled in this study at MAMC. No new patients enrolled during FY02. Follow up continues as per study protocol.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/112                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Post-operative Shoulder Pain: A Prospective Randomized Trial Comparing the Pain Infusion Pump to the Pre-induction Interscalene Block |  |                                      |
| <b>Principal Investigator:</b> CPT Joshua P. Herzog, MC   |  |                                      |
| <b>Department:</b> Surgery/Orthopedic Surgery   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> LTC Edward D. Arrington, MC; MAJ Daniel W. White, MC  |  |                                      |
| <b>Keywords:</b> Shoulder surgery, pain control infusion pump, pain management, intrascapular block   |  |                                      |
| <b>Start Date:</b><br>6/26/2001   | <b>Est. Completion Date:</b><br>Feb 02 | <b>Periodic Review:</b><br>8/27/2002 |

**Study Objective:** Determine the efficacy of the pain control infusion pump (PCIP) in controlling post-operative pain in patients undergoing shoulder surgery.

**Technical Approach:** The next 50 consecutive patients who are scheduled to undergo elective shoulder surgery to address subacromial impingement syndrome with or without a rotator cuff tear; or, acromio-clavicular degenerative disease, who meet induction criteria will be advised of the nature of the study and, upon agreement, will be entered in the study. Once consent is obtained, a randomization table will be utilized to assign the patients to Group A (pain control infusion pump) or Group B (pre-induction interscalene block). The time of determination of randomization will be in the preoperative evaluation. Patients in Group A will undergo surgery and then have a BREG MP 130 Multiport Catheter placed in the subacromial space. The catheter will be attached to the BREG 3000 Pain Control Infusion Pump with a standardized dose of 0.5% Marcaine. Patients in Group B will undergo a standardized pre-induction interscalene block utilizing the current standard technique by the anesthesia provider with 0.5% Marcaine. All patients will receive standardized anesthesia during the procedure and will spend the night of surgery in the overnight observation unit, as is our current standard of care. All patients will be given a PCA with intravenous narcotics overnight, which is the current Madigan Orthopedics standard procedure. There will be "on demand" dosage with no continuous dosing settings on the PCA device. The dose of narcotic used overnight will be recorded. During the hospital stay, the computerized inpatient record will serve as a record of use of pain medications, nausea medications, and difficulties overnight. On the day after surgery, the surgeon who performed the surgery will administer the first questionnaire. This questionnaire will consist of a 10-centimeter visual analog scale for pain, nausea, and pain control satisfaction as well as narcotic and non-narcotic analgesic use tabulation. The visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time of surgery to the present. This form will be collected by the surgeon and placed in the study file located in the orthopedic clinic research data collection office. The patient will be instructed to return for a follow-up appointment at seventy-two to ninety-six hours for operative site evaluation. They will be asked to keep a running total of all narcotic and non-narcotic pain medications used from the time of discharge until the follow-up appointment for wound evaluation. All patients will follow-up in the clinic at seventy-two to ninety-six hours for operative site evaluation. At this time, the patients in Group A will have the pain control infusion pump catheter removed from the shoulder. At this time, the number of narcotic and non-narcotic pain medications utilized will be totaled. The patient will be administered the same questionnaire used previously. Again, the visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time discharge to the present. The questionnaire will again be collected and added to the file in the orthopedic clinic. The patients will be asked to keep a running total of all narcotic and non-narcotic pain medications used from the time of the first follow-up appointment until the follow-up appointment seven to eight days after surgery. All patients will subsequently follow-up at seven to eight days after surgery for completion of the surgery data and to evaluate the operative site. Again, the same questionnaire

will be administered. Again, the visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time discharge to the present. The questionnaire will again be collected and added to the file in the orthopedic clinic. After ten patients have completed the three questionnaires, a power analysis will be performed on the data collected. The data analyzed will include comparison of visual analog scores for pain, nausea, and overall pain control satisfaction. A direct comparison of amount of narcotic and non-narcotic pain medications will also be conducted. Based on the statistical analysis and the power analysis, the study population size will be determined based on the number of patients that will be required to achieve statistically significant results. The study will then be continued until the appropriate number of patients has been enrolled. Any patient that develops a complication during the study period will be evaluated at the time of the onset of the complication. The complication will be evaluated and treated in accordance with the current standard of care. All data regarding the complication will be collected and maintained as part of the study data. Complications will be continuously followed and data collected until the condition has been resolved, stabilizes, or the study is concluded.

**Progress:** Fifteen subjects enrolled in this protocol at MAMC during FY 02. Enrollment had been sporadic due to deployment of the staff associate investigator immediately following IRB approval. Due to low enrollment, no preliminary results are available at this time. Protocol was amended to change the pump used from Breg 3000 to "On'Q Pain Management System" due to difficulty maintaining adequate pressure after priming the Breg 3000. Also, CPT Herzog assumed the role of PI for this protocol following the PCS of its original PI, MAJ White.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/066                 | <b>Status:</b> Completed             |
| <b>Title:</b> Healing of Tibial Stress Fractures Using Pulsed Electromagnetic Field (PEMF) Therapy   |  |                                      |
| <b>Principal Investigator:</b> CPT Karin A . Johnson, MC   |  |                                      |
| <b>Department:</b> Surgery/Orthopedic Surgery  | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC (Ret) Richard A. Sherman, Ph.D.; COL Nancy E. Henderson, SP; 1LT Kristine A. Youngstom, SP; Jerome Billingsley, M.D.; MAJ Susan Ishikawa, MC |  |                                      |
| <b>Keywords:</b> pulsed electromagnetic fields, stress fractures, treatment, military specific   |  |                                      |
| <b>Start Date:</b><br>4/25/2000  | <b>Est. Completion Date:</b><br>Dec 01 | <b>Periodic Review:</b><br>4/23/2002 |

**Study Objective:** To determine whether application of non-thermal, pulsed high peak power, high frequency, electromagnetic energy (PEMF) over the tibial stress fracture site used in conjunction with standard therapeutic approaches, reduces the amount of shin pain and increases endurance on the treadmill in relation to those receiving standard treatments with sham PEMF's.

**Technical Approach:** This study is a double-blind, placebo controlled study of active duty soldiers but with tightly controlled outcome measures. All subjects will receive the standard treatment in addition to PEMF or sham and will begin participation within 30 days of initial complaint after confirmation of stress fracture diagnosis by both physical findings and bone scan. Prior to initial exposure, each subject will fill out a standardized questionnaire which assesses ability to function in the work and home environment in relation to lower limb pain and disability. Each will also be evaluated for duration of walking on a treadmill until discomfort to standardize assessment of pain and endurance, and will have their bone density measured. Subjects will be randomly assigned to be exposed to either a PEMF generator putting out actual fields or an inactive (sham) generator. This will be an entirely double-blind study as the subjects will not be able to tell which group they are in because the devices sound the same and because the patients cannot feel the machine operating. The physical therapy technician who operates the device will know which generator each subject is exposed to but will not know which generator is putting out actual fields and which is the sham. The physical therapists and physician doing the evaluations will have no idea which group the patients are in. The function questionnaire and the treadmill test will be repeated at the end of the two week exposure period and then four weeks and six months after. A power analysis shows that 33 subjects will be needed in each group assuming that the actual exposure group will do better than the placebo group (one-tailed test) and that an 80% chance of finding a difference between the two groups at a 0.05 level of significance is sufficient to perform the study. Eighty subjects will be recruited to begin the study to permit a reasonable 15% dropout rate.

**Progress:** A total of 47 subjects enrolled in this study at MAMC. Of these, 24 completed all portions of the study, to include six month follow-up. The study was halted when an analysis of the data showed no difference between the treated group and the sham group at either the six week or six month follow-up. An additional five subjects has completed the six week follow-up at the time the study was halted. The remaining 18 subjects were lost to completion of the study primarily due to unit and personal time constraints. There were no adverse events reported during the study. Preliminary data analysis, using Mann-Whitney U (nonparametric with two independent samples) demonstrated no significant difference between the treatment and sham group. The average pain scores and lower limb disability scores were not statistically different between the groups. Both groups did show improvement in pain and disability over the course of treatment; however, the study was halted as the data showed no benefit to the subjects.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/009 | <b>Status:</b> Completed |
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**Title:** Positional Assessment of the Maxwell-Brancheau Arthroeresis Implant on the Subtalar Joint Using Three-Dimensional Surface Computed Tomography

**Principal Investigator:** Richard O. Jones, DPM

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** Brent A. Clark, DPM; MAJ Jay F. Wigboldy, MC; LTC Doug A. Vermillion, MC; LTC Morgan P. Williamson, MC

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**Keywords:** Subtalar arthroeresis

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**Start Date:**

10/24/2000

**Est. Completion Date:**

Jan 01

**Periodic Review:**

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**Study Objective:** To provide evidence that will help answer the following question: what position, relative to the articular facets of the subtalar joint, does the MBA arthroeresis device assume when placed according to manufacturer's guidelines.

**Technical Approach:** Six patients will be enrolled in this study. Patient's surgeries have all been performed by the same surgeon and he will evaluate records individually and identify each patient for inclusion in the study. Scans will be performed and the results will be reported individually for each subject foot as well as collectively for the group. At the time of the CT, each patient will complete a post-operative questionnaire. The primary investigator will complete the AOFAS hindfoot score for each patient at this time.

**Progress:** The protocol has been reported as completed with seven patient enrolled. An abstract is not yet available.

### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 97/095                  | <b>Status:</b> Terminated            |
| <b>Title:</b> Delayed versus Immediate Open Repair of Achilles Tendon Rupture; A Randomized Prospective Trial   |  |                                      |
| <b>Principal Investigator:</b> CPT Glenn J. Kerr, MC  |  |                                      |
| <b>Department:</b> Surgery/Orthopedic Surgery   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ John G. DeVine, MC; CPT George K. Bal, MC; LTC John D. Pitcher Jr., MC; MAJ Robert V. Williamson, MC; COL Frederic L. Johnstone, MC |  |                                      |
| <b>Keywords:</b> Achilles tendon, delayed versus immediate repair, military specific  |  |                                      |
| <b>Start Date:</b><br>5/16/1997   | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>8/21/2002 |

**Study Objective:** To evaluate the differences in surgically repairing Achilles tendon ruptures immediately, or waiting 10-14 days to perform the repair.

**Technical Approach:** All patients identified with acute Achilles tendon ruptures, who are being considered for surgical repair, will be presented the option of enrolling in this study. The subjects will be randomized to one of two Groups: Group I - Immediate surgical repair (within 72 hours) of the Achilles tendon, or Group II - delayed (between 10 and 14 days) surgical repair of the tendon rupture. The patients will be randomized using a computer generated randomization table. We will initially randomize the first ten patients, and a subsequent power analysis will be performed at 6 month follow-up to insure that enough patients are enrolled to make our results significant. The next 20 patients will be randomized using a second computer generated table. The post-operative course for both Groups will be the same. The patients will be followed up at 2 week, 6 week, 9 week, 6 month, 12 month, and 24 month intervals. They will be evaluated for post-operative complications and functional outcome.

**Progress:** Investigators reported this protocol as terminated when it was noted that most of the study's enrolled subjects had moved and were subsequently "lost to follow-up" before planned post-operative assessments could be completed. This study had a total enrollment of 32 patients overall.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/015 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques

**Principal Investigator:** CPT Kurtis L. Kowalski, MC

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL Patrick St Pierre, MC; CPT Brendon R. Connolly, MC; LTC Edward D. Arrington, MC

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**Keywords:** acromioclavicular joint separations, coracoclavicular ligament, C-C ligament reconstruction, Weaver-Dunn reconstruction

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**Start Date:**

10/24/2000

**Est. Completion Date:**

Sep 00

**Periodic Review:**

9/26/2001

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**Study Objective:** Test the strength and biomechanical characteristics of native and intact coracoclavicular ligament complexes as well as various reconstructive techniques for treating high-grade acromioclavicular joint separations.

**Technical Approach:** Thirty coracoclavicular bone-ligament-bone specimens will be harvested from fresh-frozen human cadavers. Unidirectional tensile loading will be performed with the Instron device. Tensile loading will be applied to the clavicle at a uniform rate until failure of the coracoclavicular ligament complex occurs. The coracoclavicular ligament will then be reconstructed using either gracilis tendon, palmaris longus tendon, or SIS graft. The grafts will be looped multiple times under the coracoid process and over the top of the clavicle. It will be secured to itself with a #2 Ethibond suture. They will then be tested to failure as previously described. Data will be obtained from the Instron device regarding tensile strength, load to failure, stiffness, and elongation to failure. Statistical analysis will be performed using a one-way ANOVA to determine differences between groups as well as Duncan's multiple range test to determine specific differences.

**Progress:** This study remained inactive during during FY 02. Investigators had experienced technical difficulty securing the clavicle and the scapula to the Instron, and are attempting to find a better method of securing the test specimens. Work with the Instron is planned to continue during FY 03.



### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/125                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome   |  |                                      |
| <b>Principal Investigator:</b> CPT Bryant G. Marchant, MC  |  |                                      |
| <b>Department:</b> Surgery/Orthopedic Surgery  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Christopher J. Wilson, MC; LTC Edward D. Arrington, MC; CPT Brian K. Konowalchuk, MC; COL Patrick St Pierre, MC; CPT Neil C. Vining, MC  |  |                                      |
| <b>Keywords:</b> subacromial, injection, toradol, ketorolac, corticosteroid  |  |                                      |
| <b>Start Date:</b><br>8/22/2000  | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>7/23/2002 |
| <b>Study Objective:</b> To evaluate the difference in pain relief and functional outcome for subacromial impingement syndrome for patients who are treated with either a subacromial injection of corticosteroids or a subacromial injection of Ketorolac.   |  |                                      |
| <b>Technical Approach:</b> This double-blind, randomized study will enroll approximately 40 patients with uncomplicated impingement syndrome for treatment with either subacromial corticosteroids or Ketorolac. Subjects with subacromial impingement will be given either 6cc 1% lidocaine with epinephrine and 40 mg Triamcinolone (Control) or 6cc 1% lidocaine with epinephrine and 60mg injectable Toradol (Test). Patient evaluation will be done at the time of injection and at 4 weeks post-injection. |  |                                      |
| <b>Progress:</b> One subject enrolled in FY 02, for a total of 22 subjects enrolled in this study at MAMC. Subject enrollment continues.   |  |                                      |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/014 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Comparison of Instrumented Posterior Lumbar Interbody Fusion Technique: One vs Two Cages

**Principal Investigator:** MAJ Robert W. Molinari, MC

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** CPT John F. Sloboda, MC

**Keywords:** posterior lumbar interbody fusion, cage

**Start Date:**  
11/27/2001

**Est. Completion Date:**  
Sep 01

**Periodic Review:**

**Study Objective:** (1) Evaluation of fusion using one or two cages in posterior lumbar interbody fusion (PLIF), (2) evaluation of patient functional outcomes after PLIF via patient survey, (3) cost comparison of one vs two cage PLIF, and (4) assessment of complication rate in one vs two cage PLIF.

**Technical Approach:** A retrospective study of 35 patients with spondylolithesis, one or two level degenerative disk disease or one or two level lumbar spinal stenosis who underwent one or two level instrumented posterior lumbar interbody fusion with one or two cage technique. Fusion rates will be evaluated for potential decrease in fusion rate using one versus two cage technique. Cost analysis will be assessed for cost savings in use of one versus two cage technique for PLIF. Complication rate will be assessed for a potential increase in complications utilizing two versus one cage technique. Functional outcome will be evaluated using a patient outcome survey.

**Progress:** Data collection from retrospective data continues.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/015                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Outcome of Instrumented Posterior Lumbar Interbody Fusion (PLIF) with Cage for Low-Grade Spondylolithesis  |  |                         |
| <b>Principal Investigator:</b> MAJ Robert W. Molinari, MC  |  |                         |
| <b>Department:</b> Surgery/Orthopedic Surgery  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> CPT John F. Sloboda, MC  |  |                         |
| <b>Keywords:</b> posterior lumbar interbody fusion, cage   |  |                         |
| <b>Start Date:</b><br>11/27/2001   | <b>Est. Completion Date:</b><br>Sep 01 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> Evaluation of fusion and complication rate in posterior lumbar interbody fusion (PLIF) with cage for low-grade spondylolithesis and evaluation of patient functional outcome after PLIF via patient survey.  |  |                         |
| <b>Technical Approach:</b> A retrospective study of 14 patients with low-grade spondylolithesis who underwent one level instrumented posterior lumbar interbody fusion with cage. Fusion and complication rates will be evaluated and compared with current literature. Functional outcome will be evaluated using a validated patient outcome survey and whether or not full return to duty was achieved. |  |                         |
| <b>Progress:</b> This retrospective protocol is still in data gathering phase. No analysis has been done yet.  |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/056 | <b>Status:</b> Ongoing |
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**Title:** Use of Overpronation Controlling Insoles to Prevent Low Limb Pain (MRMC project #2016)

**Principal Investigator:** CPT Neil C. Vining, MC

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| <b>Department:</b> Surgery/Orthopedic Surgery | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC (Ret) Richard A. Sherman, Ph.D.; COL Nancy E. Henderson, SP; LTC John P. Gerber, SP

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**Keywords:** pain overpronation insoles soldiers, military specific

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**Start Date:**  
3/26/2002

**Est. Completion Date:**  
Feb 03

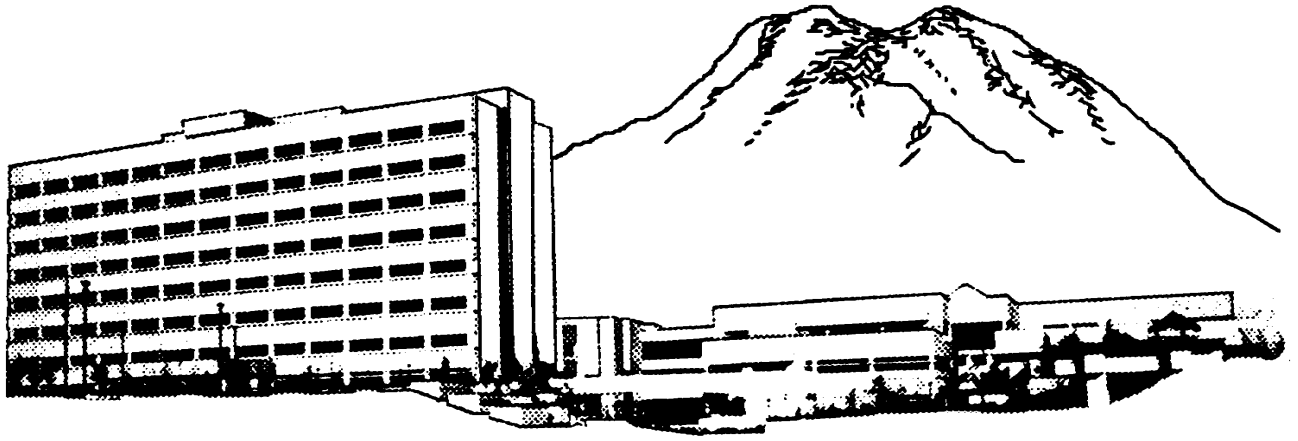
**Periodic Review:**

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**Study Objective:** To determine whether use of overpronation correcting boot and sneaker inserts reduce lower limb pain and permit increased activity relative to use of a shock absorbing insert by combat soldiers stationed at fort Lewis Washington. This is a two phase study. In the first phase, only overpronating soldiers experiencing sufficient lower limb pain to interfere with their running will participate. If at least half of the soldiers do not show at least fifty percent greater reduction in pain after using the overpronation correcting insert than those using the shock absorbing insert, the second phase will not be performed. The second phase is the same protocol but with overpronating, pain free soldiers and the outcome measure of interest is increased activity without pain.

**Technical Approach:** The research associate will screen all interested members of participating combat units at Fort Lewis who experience lower limb pain for clinically significant amounts of overpronation (a navicular drop from subtalar joint neutral to relaxed calcaneal stance measuring more than ten mm with full weight bearing while in bipedal stance). 110 soldiers will be recruited of the 520 soldiers screened. The soldiers will be randomized as they enter the study to receive either overpronation correcting or shock absorbing (placebo) insoles. Each participating soldier will fill in a pre-participation questionnaire (concerning prior history of pain, activity, etc.) and keep a log of pain and activity for a month. They will then be issued two identical pairs of insoles. (one for the boots and one for the sneakers) to use continuously for two months after which they will keep the log for an additional month. Each will fill out a use and effectiveness questionnaire at the end of participation. If at least half of the soldiers do not show at least 50% greater reductions in pain after using the overpronation correcting insert than those using the shock absorbing insert, the second phase will not be performed. The second phase is the same protocol but with overpronating, pain free soldiers and the main outcome measure of interest for this phase is increased activity without pain.

**Progress:** This study has not yet received final approval, pending approval of Ibeen initiated at MAMC, pending completion IRB approval process.



## **Detail Summary Sheets**

# **Otolaryngology Service, Department of Surgery**

### Detail Summary Sheet

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|                        |                        |                        |
|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/139 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** Use of Elastin Patch for Repair of Traumatic Tympanic Membrane Perforations in the Chinchilla (*Chinchilla laniger*)

**Principal Investigator:** CPT James V. Crawford, MC

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**Department:** Surgery/Otolaryngology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Paulino E. Goco, MC; CPT Sam Y. Kim, MC

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**Keywords:** tympanic membrane perforations, chinchilla langier, elastin patch, tympanic membrane repair

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**Start Date:**  
9/19/2001

**Est. Completion Date:**  
May 04

**Periodic Review:**  
9/19/2001

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**Study Objective:** (1) Laser soldering of liquid albumin coupled with elastin can provide an immediate functional repair of tympanic membrane perforations (2) that elastin biomaterial can facilitate tympanic membrane repair in acute tympanic membrane perforations (3) that elastin biomaterial compares favorably with traditional paper patch techniques In non-technical terms state the objective of this protocol, or the hypothesis to be accepted or rejected.

**Technical Approach:** This study will utilize an elastin biomaterial (Oregon Medical Laser Center, Portland, OR) to repair acute TM perforations in an animal model (*Chinchilla langier* ). TM perforations will be created with a thermal loop under general anesthesia and then repaired immediately utilizing elastin biomaterial with or without laser-activated tissue adhesive. A comparison study with the standard paper patching technique will also be conducted in parallel. We anticipate that the elastin biomaterial will prove to be a functional patch material for TM perforations, as confirmed by tympanometry, and will promote rapid healing. If this is true, there is potential for application to the acute repair of traumatic TM perforations in humans, which can result in decreased morbidity and accelerated return to full-functioning capacity.

**Progress:** A total of 19 chinchillas were utilized during FY02. 2 animals were sacrificed after establishing feasibility of the overall study. 1 chinchilla died after an altercation with another chinchilla. The remaing 17 were divided amongst three groups: 1) tympanic perforation patched with paper, 2) tympanic perforation patched with elastin and solder, and 3) tympanic perforation patched with elastin alone. The animals were followed for six weeks and sacrificed. Results relating to tympanic membrane integration and integrity of repair are pending.

### Detail Summary Sheet

|   |  |                         |
|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/072                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Double Blind Placebo Controlled Trial of Montelukast for the Prevention of Recurrence of Chronic Nasal/Sinus Polyposis and Chronic Hyperplastic Sinusitis - A Follow-up Study |  |                         |
| <b>Principal Investigator:</b> CPT Wayne J. Harsha, MC  |  |                         |
| <b>Department:</b> Surgery/Otolaryngology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> CPT Jamie R. Steger, MC; LTC John C. Walker, MC; MAJ Douglas M. Sorensen, MC  |  |                         |
| <b>Keywords:</b> nasal sinus polyps chronic hyperplastic sinusitis montelukast recurrence   |  |                         |
| <b>Start Date:</b><br>5/28/2002   | <b>Est. Completion Date:</b><br>Nov 03 | <b>Periodic Review:</b> |

**Study Objective:** To ascertain if combining montelukast with topical nasal steroids results in less recurrences and/or slower recurrences of nasal polyposis and chronic hyperplastic sinusitis.

**Technical Approach:** This is a double blinded, placebo controlled trial to ascertain if the adjunctive therapy of LTRA, montelukast, will lead to less and slower recurrence of CHS/NP postoperatively. Sixty patients (30 in each arm) will be recruited from Family Practice, Adult Primary Care, Pulmonary Medicine, Allergy and ENT with clinical chronic hyperplastic sinusitis and /or nasal/sinus polyps. Baseline evaluation will include history, physical examination with nasorhinoscopy, sinus CT, nasal acoustic rhinometry, skin testing to a standard panel of aeroallergens, IgE, Chem 10 panel, CBC, quantitative immunoglobulins and Rubella titer. All subjects will have therapy initiated with nasal lavage and nasal fluticasone propionate 50 MCG/puff, 2 puff each nostril bid postoperatively. They will be randomized postoperatively to receive either placebo or montelukast 10 mg/day in double-blinded controlled fashion. Follow up evaluations with symptom scores, acoustic rhinometry and rhinoscopy will be performed at 3, 6 and 12 months. Patients will have follow up sinus CT at 6 and 12 months postoperatively. Comparison will be made to their baseline data and between the active and placebo groups. Acoustic rhinometry, symptom scores and standardized grading of sinus CT were chosen to facilitate gathering of objective data that would be comparable. The unpaired T-test will be used to compare the placebo and treatment arms with regards to the CT scoring, polyp scores, symptom scores and acoustic rhinometry.

**Progress:** A total of two patients have been enrolled in the study since it was approved. They have both undergone FESS and are now on the study medication/placebo. In addition, we have another patient who has agreed to be in the study and is scheduled to see me within the next two weeks to sign the consent and undergo the preoperative evaluations. There have been no adverse outcomes, and no patients have withdrawn from the study.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/059 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Initial Investigation into the Effects of Sleep Deprivation Using the Sinus Surgery Simulator

**Principal Investigator:** CPT Sam Y. Kim, MC

**Department:** Surgery/Otolaryngology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paulino E. Goco, MC; Vincent D. Eusterman, MD

**Keywords:** sinus surgery surgical simulation sleep deprivation

**Start Date:**

3/26/2002

**Est. Completion Date:**

Aug 02

**Periodic Review:**

**Study Objective:** To evaluate sleep deprivation and surgeon performance using the sinus surgery simulator.

**Technical Approach:** Sleep deprivation is inherent in residency training programs. Past studies and experiences have shown that sleep deprivation can be detrimental to patient care. Other studies have shown the opposite. By utilizing validated surgical stimulation, it is now possible to directly assess the impact of fatigue by comparing resident physicians before and after sleep deprivation. The use of the simulator allows for consistent and objective assessment without involving a live patient in the study. Madigan Army Medical Center has one of three sinus surgical simulators in the world. The goal of this protocol is to investigate the impact of sleep deprivation on resident physicians, as documented by sinus surgical simulation.

**Progress:** The protocol was based on using the endoscopic sinus simulator for measurement of hand eye coordination skills after sleep deprivation. The sinus simulator was, until very recently, non functional. The simulator is now operational, and I plan to start the protocol as soon as my schedule permits.



### Detail Summary Sheet

|   |                       |                           |
|---|-----------------------|---------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 99/050 | <b>Status:</b> Terminated |
| <b>Title:</b> Pediatric Bronchoesophagology Laboratory Using Swine (Sus scrofa) |                       |                           |
| <b>Principal Investigator:</b> MAJ Douglas M. Sorensen, MC                      |                       |                           |
| <b>Department:</b> Surgery/Otolaryngology                                       |                       | <b>Facility:</b> MAMC     |
| <b>Associate Investigator(s):</b> Andrew Inglis, M.D.; MAJ Andrew B. Silva, MC  |                       |                           |
| <b>Keywords:</b> Bronchoesophagology, pediatric, animal teaching model          |                       |                           |

|                                 |  |                                      |
|---------------------------------|--|--------------------------------------|
| <b>Start Date:</b><br>3/23/1999 | <b>Est. Completion Date:</b><br>Mar 02 | <b>Periodic Review:</b><br>5/18/2000 |
|---------------------------------|--|--------------------------------------|

**Study Objective:** To familiarize the junior otolaryngology residents at MAMC and the UW and the Pediatric Surgery fellows at CHMC, with the endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children. This would include familiarization with esophageal and tracheal foreign body removal, rigid and flexible endoscopic techniques and endobronchial laser use. Familiarity with these techniques would allow an increased margin of safety for children undergoing these procedures and better prepare the endoscopist to assist and then perform these procedures when necessary. Increased endoscopic training experiences will increase operative efficiency and minimize the potential operative risks involved in these procedures.

**Technical Approach:** This is a 4-hour afternoon laboratory session. The LARS, under the supervision of an attending veterinarian, will administer the anesthesia. During this time, 3 pigs will be anesthetized under general anesthesia using IM Rompun/ketamine (2.2mg/kg 20mg/kg). LARS will then obtain intravenous access. Once an adequate plan of anesthesia has been reached, the course participants will perform rigid and flexible bronchoscopy with extraction of a foreign body and esophagoscopy under the supervision of an attending endoscopist. In order to maximize the number of procedures that can be performed within the shortest amount of anesthetic exposure, three live animal stations will be used. The first and second station will be used to teach rigid endoscopy and foreign body removal. The third station will be used to teach flexible endoscopy and foreign body removal. There will also be two additional teaching stations. One will involve instrument set up and use, while the other will involve a teaching station for removal of a safety pin.

Approximately 20 endoscopic procedures will be performed on each animal. Foreign bodies will be used that reproduce those encountered in clinical practices (peanuts, beans, Lego). The foreign bodies will be endoscopically placed and extracted from the bronchus and trachea, under direct vision of the participants and instructors. At the end of the laboratory session, the pigs will be euthanized while they are still under general anesthesia in accordance with the IAW LARS SOP for euthanasia.

All course participants will perform bronchoscopies and foreign body removal on models prior to operating on the swine. The course participants will also participate in a half-day didactic component prior to the laboratory session and will be required to undergo a post course quiz. Completion of the training will be determined by the participant's ability to successfully, and atraumatically perform a bronchoscopy and esophagoscopy with airway foreign body removal.

**Progress:** The bronchoesophagology lab has been found to be an important tool and teaching method for junior residents in Otolaryngology to learn foreign body extraction of the airway and esophagus. This lab improves resident's skills in bronchoesophagology and its value as a teaching method cannot be duplicated by any other means. This protocol reached its 3-year expiration and was terminated, 23 Mar 02. A replacement protocol has been reviewed by the IACUC and approved under a different protocol number.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 202/097      **Status:** Ongoing

**Title:** Perioperative Immunonutrition for Head and Neck Cancer: Effect on Nutritional Status and Immune Response

**Principal Investigator:** MAJ Douglas M. Sorensen, MC

**Department:** Surgery/Otolaryngology      **Facility:** MAMC

**Associate Investigator(s):** Mary S. McCarthy, RN, MNS; MAJ Douglas M. Sorensen, MC

**Keywords:** immunonutrition head and neck cancer perioperative nutrition

**Start Date:**  
7/23/2002

**Est. Completion Date:**  
Nov 05

**Periodic Review:**

**Study Objective:** To examine the effects of preoperative administration of an immune-enhanced enteral formula on nutritional status and immune response in patients having surgery for head and neck cancer, compared to patients who receive standard of care (usual diet). To monitor hospital course of all subjects for clinical outcomes of infectious complications, wound healing, gastrointestinal side effects, and immune response postoperatively. To evaluate hospital outcome at 30 days and quality of life at 3 months for all subjects.

**Technical Approach:** Patients with head and neck cancer are at great risk for malnutrition preoperatively, impaired host defenses and poor wound healing postoperatively. Specific nutrient substrates such as omega-3 fatty acids, arginine, glutamine and nucleotides have unique metabolic and immunologic benefits for the patient who is subject to conditions that result in immunosuppression such as major surgery, sepsis or malignancy. The capacity for nutrients to modulate the actions of the immune system and to affect clinical outcome has become an important issue in clinical practice and public health. Recent studies have consistently shown that patients receiving immune-enhancing nutrition (IEN) have a significant improvement and faster recovery of several immune and inflammatory parameters, but this occurs only after 5 to 7 days of enteral formula delivery. By providing an immune-enhancing diet in the preoperative period, the high risk patients will experience optimal therapeutic response at the time the body needs it most, immediately following surgery. The specific aim of this prospective randomized study is to examine the benefits of perioperative immunonutrition in patients undergoing major head and neck surgery by comparing patients who receive immune-enhancing nutrition preoperatively to those who receive standard of care or usual diet. Immunologic and nutritional outcomes will be measured at four different time points. Patients consenting to participate in this study will have a PEG tube or Dobhoff tube and will receive either immune-enhanced formula (Impact) or standard of care (usual diet) for a period of 7 days before surgery. Both groups will receive IEN for 7 days postoperatively. The clinical pathway for head cancer patients standardizes many aspects of care including preoperative gastrostomy tube placement and routine speech pathology and dietitian consultation. Primary outcomes include nutritional status based on albumin, pre-albumin, nitrogen balance, subjective global assessment and body fat analysis and immunologic response measured by IL-6, IL-2 receptors alpha and IL-1 soluble receptors. Secondary outcomes include wound healing, monitored with transcutaneous oxygen measurements and a scoring tool and infectious complications. A disease-specific quality of life (QOL) too, the Head and Neck Cancer QOL instrument will provide some data regarding quality of life in this population over a three month period. Comparison of baseline characteristics and immune biomarkers between groups will be measure by the Student's test or Fisher's exact test as appropriate. Time variation of cytokine release and nutritional status of the two groups will be compared using repeated measures analysis of variance.

**Progress:** Study recently received approval and has not started enrolling patients yet.

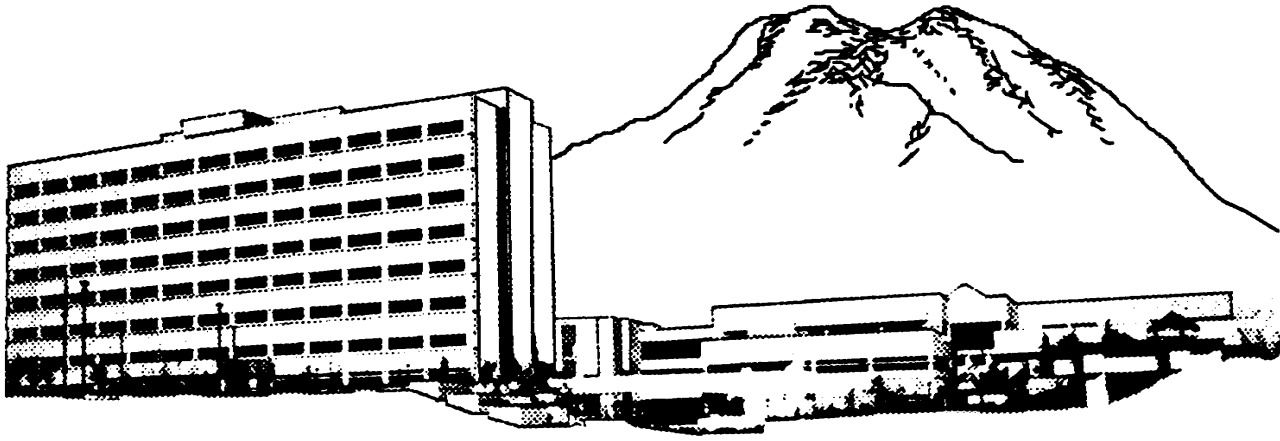
### Detail Summary Sheet

|   |  |                                      |
|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/093                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Double Blind Placebo Controlled Trial of Montelukast for the Treatment and Prevention of Recurrence of Chronic Nasal/Sinus Polyposis and Chronic Hyperplastic Sinusitis |  |                                      |
| <b>Principal Investigator:</b> CPT Jamie R. Steger, MC  |  |                                      |
| <b>Department:</b> Surgery/Otolaryngology   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Douglas M. Sorensen, MC; LTC John C. Walker, MC   |  |                                      |
| <b>Keywords:</b> nasal/sinus polyps, chronic hyperplastic sinusitis, montelukast  |  |                                      |
| <b>Start Date:</b><br>4/24/2001   | <b>Est. Completion Date:</b><br>Dec 01 | <b>Periodic Review:</b><br>8/27/2002 |

**Study Objective:** To ascertain if combining montelukast with topical nasal steroids results in more rapid resolution of nasal polyposis and chronic hyperplastic sinusitis.

**Technical Approach:** This is a prospective, randomized, double blinded, placebo controlled trial to ascertain if adjunctive therapy of a LTRA, montelukast, will lead to more rapid and complete resolution of chronic hyperplastic sinusitis with nasal or sinus polyposis. Sixty patients will be recruited from Family Practice, Adult Primary Care, Pulmonary medicine, Allergy, and ENT with clinical chronic hyperplastic sinusitis and nasal/sinus polyps. Baseline evaluation will include history, physical examination with rhinoscopy, symptom scores, sinus CT, nasal acoustic rhinometry, skin testing to a standardized panel of aeroallergens, IgE, chem 10 panel, CBC, quantitative immunoglobulins, and tetanus titer. All subjects will have therapy initiated with nasal lavage and nasal fluticasone propionate 50 ucg/puff, 2 puff each nostril bid. They will then be randomized to receive either placebo or montelukast 10 mg/day in double-blinded controlled fashion. Follow up with evaluations with symptom scores, acoustic rhinometry, and rhinoscopy and sinus CT will be performed at 12 weeks. Comparison will be made to their baseline data and between the active and placebo groups. Acoustic rhinometry, symptom scores, standardized rhinoscopy scores and standardized grading of sinus CT were chosen to facilitate gathering of objective data that would be comparable.

**Progress:** This protocol enrolled 12 patients total with 9 patients enrolled during FY02 . There were no serious adverse events. The protocol was amended to change the upper age limit for study participants from 65 to 80. No conclusions have been drawn to date. This study remains ongoing.



## **Detail Summary Sheets**

### **Plastic Surgery Service, Department of Surgery**

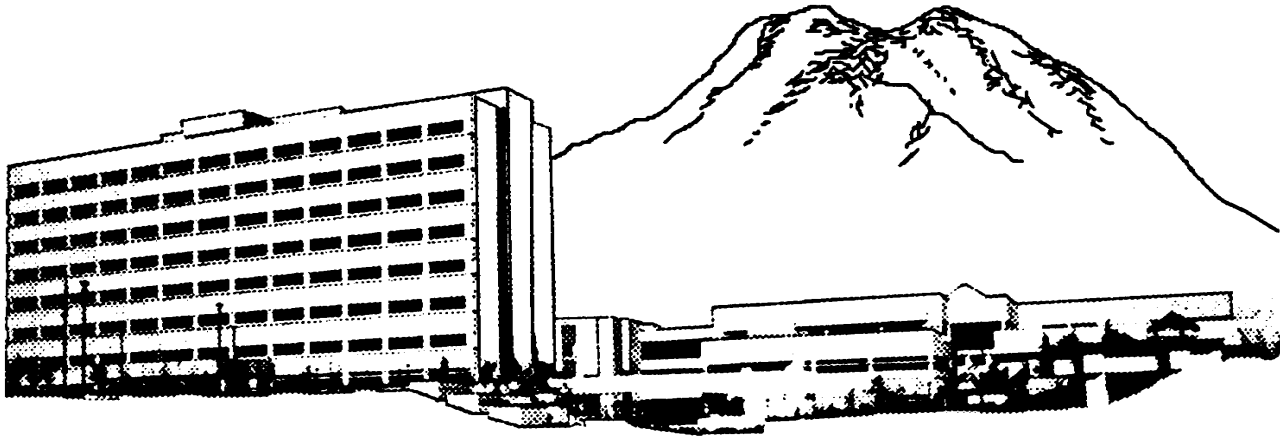
### Detail Summary Sheet

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|--|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/025                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> Microsurgery Training Utilizing The Rat ( <i>Rattus norvegicus</i> ) as a Teaching Model |  |                                      |
| <b>Principal Investigator:</b> COL Stiles T. Jewett, Jr., MC   |  |                                      |
| <b>Department:</b> Surgery/Plastic Surgery   |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> COL Frederic L. Johnstone, MC  |  |                                      |
| <b>Keywords:</b> Microsurgery training rats surgery  |  |                                      |
| <b>Start Date:</b><br>12/5/2001  | <b>Est. Completion Date:</b><br>Dec 04 | <b>Periodic Review:</b><br>12/5/2001 |

**Study Objective:** The establishment of a microsurgical laboratory utilizing appropriate inanimate materials, and anesthetized rats for the teaching and practice of micro surgical techniques will significantly enhance the skills of MAMC surgical staff and residents. It will also correct a deficiency in the Orthopedic Surgery Residency Program (lack of formal microsurgery training) identified by Residency Review Committee for Orthopedics. Availability of such a laboratory for skill maintenance and enhancement is the standard at teaching institutions that perform microsurgery.

**Technical Approach:** This is a micro-surgical training procedure using fully euthanatized subjects.

**Progress:** Commencement of the study is awaiting approval of CEEP funding of equipment for the planned Microsurgery Laboratory. Initially, it is not expected that any human subjects will be involved as this will be primarily an animal model surgical skills lab.



## **Detail Summary Sheets**

### **Urology Service, Department of Surgery**

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/057                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Phase III, Randomized, Double Blind, Multicenter and Multinational Study to Determine the Efficacy and Safety of Tolterodine Prolonged Release Capsules in Children 5 to 10 Years of Age with Symptoms of Urge Urinary Incontinence, Suggestive of Detrusor Instability  |  |                         |
| <b>Principal Investigator:</b> LTC Robert C. Allen, MC   |  |                         |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Raymond A. Costabile, MC   |  |                         |
| <b>Keywords:</b> MSU - mid stream urine (specimen), UTI - Urinary Tract Infection detrusor instability tolterodine children  |  |                         |
| <b>Start Date:</b><br>3/26/2002  | <b>Est. Completion Date:</b><br>Jun 04 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> The primary objective is to compare the clinical efficacy of tolterodine PR 2 mg and placebo regarding the change in number of daytime incontinence episodes/week after 12 week of treatment in children 5 to 10 years of age with symptoms of urge urinary incontinence, suggestive of detrusor instability. The secondary objectives are: a) To compare the clinical efficacy of tolterodine PR 2 mg qd and placebo regarding change in mean number of micturitions per 24 hours, mean urinary volume voided per micturition, number of nights with nocturnal enuresis per week, parent/guardian - reported quality of life and regarding treatment satisfaction. b) To compare tolterodine PR 2 mg qd and placebo with regard to safety and tolerability  |  |                         |
| <b>Technical Approach:</b> This is a double blind, randomized, placebo-controlled, multinational and multicenter study with two parallel groups in children five to ten, male or female with symptoms of urge urinary incontinence, suggestive of detrusor instability. Each patient will be randomized to receive either tolterodine PR 2mg qd or placebo for 12 weeks, in the ratio of 2:1. The total expected duration of patient participation is 13-14 weeks divided as follows: 1 week wash out (if required), one week run in, and study treatment for 12 weeks. The patient will be given a micturition diary to be completed. The parent/guardian will be asked to complete the Pediatric Enuresis Module questionnaire to assess the Quality of Life and patient satisfaction survey. A PVR with ultrasonography will be performed. Changes of concomitant medications will be recorded. Adverse events observed. The child will have an ECG done after the completion of the study medication prior to removal from the study. For patients not participating in the continuation study there will be a follow-up telephone contact 1 week after the patient's discharge from the study and, in the case of unresolved adverse events, a contact will be made 2 weeks after the last dose. All drug related and serious adverse events will be followed until resolved, declared stable or chronic. |  |                         |
| <b>Progress:</b> Four patients have been enrolled into this study here at MAMC. All four have received drug, two have completed follow-up and two are still being followed. Patient follow-up will continue during FY02.   |  |                         |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/058 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** An Open Label, Multicenter, Multinational Study to Determine the Safety and Efficacy of Tolterodine Oral Solution in Children with Symptoms of Urge Urinary Incontinence Suggestive of Detrusor Instability

**Principal Investigator:** LTC Robert C. Allen, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Raymond A. Costabile, MC

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**Keywords:** MSU - mid stream urine (specimen), UTI - Urinary Tract Infection, ECG-  
Electrocardiogram detrusor instability

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**Start Date:**  
3/26/2002

**Est. Completion Date:**  
Jun 04

**Periodic Review:**

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**Study Objective:** The primary objective is to study the safety and tolerability of tolterodine oral solution (1 mg b.i.d) during 6 months of treatment in children 5 to 10 years of age with symptoms of urge urinary incontinence, suggestive of detrusor instability. The secondary objective is to document the clinical efficacy and perform additional safety assessments.

**Technical Approach:** This is an open-label, multinational (USA and CANADA), multicenter study to determine the safety and efficacy of tolterodine oral solution (1 mg b.i.d) in children ages five to ten male or female with symptoms of urge urinary incontinence, suggestive of detrusor instability. The total expected duration of patient participation (Visit 1-5) is 27-28 weeks, divided as follows; 1-week wash out (9f required), 1 week run in, followed by study treatment for 6 months. The inclusion/exclusion criteria will be reviewed and informed consent will be obtained as well as patient history, physical exam and 12 lead ECG. A venous blood sample will be done, ultrasonography bladder scan and a micturition diary will be given to the patient. Parent/guardian will complete a "bladder difficulty" quality of life questionnaire. An MSU sample will be obtained for dipstick urinalysis, culture and microscopy to ascertain retrospectively that the patient was not suffering from UTI at the time of completing the diary. Concomitant medications will be reviewed and any serious adverse events will be recorded and a treatment satisfaction questionnaire will be completed by parent/guardian. All drug related and serious adverse events will be followed until resolved, declared stable or chronic.

**Progress:** Three patients have been enrolled into this study at MAMC. Two patients have received drug, one patient remains in screening. Enrollment is still open. Follow-up will continue for FY02.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/047

**Status:** Ongoing

**Title:** Mechanical Oral Bowel Preparation for Urinary Diversion Surgery: A Prospective Evaluation of Patient and Surgeon Satisfaction

**Principal Investigator:** LTC Robert C. Allen, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** COL Raymond A. Costabile, MC; MAJ Sunil K. Ahuja, MC; LTC Henry E. Ruiz, MC; MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC; MAJ Thomas L. Poulton, MC; CPT Leah P. McMann, MC

**Keywords:** multicenter, bowel preparation, urinary diversion surgery, patient satisfaction

**Start Date:**  
2/26/2002

**Est. Completion Date:**  
Oct 03

**Periodic Review:**

**Study Objective:** To compare the satisfaction of both physicians and patients with 2 established mechanical bowel cleansing regiments using a brief questionnaire.

**Technical Approach:** All patients undergoing urologic surgery requiring mechanical bowel preparation (urinary diversion and bladder augmentation) who agree to participate in the study will be randomly assigned to one of two mechanical bowel preparations. The first consists of 2 doses of oral Fleet's Phosphosoda (45cc) at 1500 and 2100, the day before surgery. The second group will use 4 liters of oral polyethylene glycol between 0900 and 1200, the day before surgery. Both bowel preparations are considered standard of care. Postoperatively, all patients will fill out a questionnaire detailing their satisfaction and tolerance of their bowel preparation. In addition, all operating physicians will fill out a questionnaire detailing their satisfaction with the bowel preparation. All patients will undergo chemistry 10 panel at their preoperative visit and immediately postoperatively.

**Progress:** 6 patients have been enrolled into this study at MAMC during FY02. All 6 patients have been completed, enrollment remains open for 4 more patients.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/085 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Open Label Extension and Long Term Safety Study of Tolterodine PR Capsules in Children 5 to 11 Years of Age with Symptoms of Urge Urinary Incontinence, Suggestive of Detrusor Instability

**Principal Investigator:** LTC Robert C. Allen, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
|------------------------------------|-----------------------|

**Associate Investigator(s):** MAJ Raymond S. Lance, MC; COL Raymond A. Costabile, MC; LTC Henry E. Ruiz, MC; MAJ Thomas L. Poulton, MC

**Keywords:** tolterodine children urge urinary incontinence detrusor instability

**Start Date:**  
6/25/2002

**Est. Completion Date:**  
Aug 04

**Periodic Review:**

**Study Objective:** The objective is to assess the long-term safety of tolterodine PR capsules in children 5-11 years of age with symptoms of urge urinary incontinence, suggestive of detrusor instability.

**Technical Approach:** This is an open label, long-term study with children ages five to eleven, male or female with symptoms of urge urinary incontinence, suggestive of detrusor instability, that previously completed the DETAPT-0581-008 and would like to continue on a regimen of tolterodine PR capsules. Each patient who chooses to continue will receive tolterodine PR capsules 2 mg qd for one year. Inclusion/exclusion criteria will be reviewed and informed consent obtained. Patient history will be collected and recorded, preliminary testing done and concomitant medications will be recorded. Serious adverse events and any interruptions to medications will be recorded at each visit. Patient compliance will also be recorded. This study will be collecting safety data from all patients that received at least one dose of study medication during this continuation study.

**Progress:** This study has not yet begun here at MAMC during FY02. There are 4 patients potentially pending enrollment.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/094                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A 6-Week, Double-Blind, Placebo Controlled, Randomized, Parallel Group, Multicenter, Multidose Study of the Efficacy and Safety of KW-7158 in Patients with Overactive Bladder Symptoms of Increased Urinary Frequency, Urgency, and Urge Incontinence   |  |                         |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC  |  |                         |
| <b>Department:</b> Surgery/Urology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> LTC Robert C. Allen, MC; MAJ Raymond S. Lance, MC; MAJ Thomas L. Poulton, MC   |  |                         |
| <b>Keywords:</b> Bladder Outlet Obstruction Electrocardiogram Hormone Replacement Therapy Urinary Tract Infection  |  |                         |
| <b>Start Date:</b><br>7/23/2002  | <b>Est. Completion Date:</b><br>Sep 04 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> The primary objective of this study is to evaluate the efficacy of KW-7158 compared with placebo in patients with overactive bladder symptoms of increased urinary frequency, urgency and urge incontinence after repeated daily administration for 6 weeks and to establish the most appropriate dose of KW-7158 for subsequent clinical studies.   |  |                         |
| <b>Technical Approach:</b> This study will be a phase II, multicenter, double-blind, placebo controlled randomized study with a 2-3week washout that incorporates a 1-week placebo run-in, in males and females 18 years of age and older with overactive bladder symptoms of increased urinary frequency, urgency and urge incontinence. Approximately 20 patients will be enrolled in Part A of this protocol here at MAMC. Patients will attend the clinic on 7 occasions. Before any study procedures are conducted the patient will read the informed consent and all questions and concerns will be answered by the primary investigator. The patients taking part in the study will be withdrawn from existing medication that may affect the symptoms of overactive bladder (except hormone replacement therapy and local estrogen therapy if started >2 months prior to screening visit). The patients will be trained in keeping a bladder diary, a medical history and prior therapies will be recorded. A complete physical will be done with vital signs, blood and urine samples will be drawn for laboratory tests will be performed. A uroflometry and post-void residual volume will be done by ultrasound and a digital electrocardiogram will be performed. The patient will be expected to bring the diary and report any serious adverse effects during the following visits. A quality of life questionnaire will be completed. Patients will return to the clinic 1 week after the last administration of study drug for their follow-up visit (visit 7) and the following assessments and procedures will be performed: A urine sample will be taken for laboratory testing concomitant medication and adverse events will be check and recorded, and if necessary, a physical exam will be completed and vital signs will be recorded. The primary end point for clinical symptoms will be the change from base line to Visit 6 in mean number of micturations (including incontinence) per 24 hours. The analysis of this end point will be carried out using an ANCOVA and a LOCF analysis. |  |                         |
| <b>Progress:</b> During FY02, one patient has been enrolled into this study at MAMC, still remains in screening. Patient enrollment remains open and follow-up will continue for FY02.   |  |                         |

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 202/096      **Status:** Ongoing

**Title:** A Multicenter, Open-Label Extension, Flexible Dose Escalation Study to Evaluate Self-Esteem and Overall Relationships in Men with Erectile Dysfunction Treated with Viagra (sildenafil citrate) in the United States, (Protocol Number A1481120)

**Principal Investigator:** COL Raymond A. Costabile, MC

**Department:** Surgery/Urology      **Facility:** MAMC

**Associate Investigator(s):** LTC Robert C. Allen, MC; LTC Henry E. Ruiz, MC; MAJ Raymond S. Lance, MC; CPT Leah P. McMann, MC; MAJ Thomas L. Poulton, MC

**Keywords:** ED-erectile dysfunction, sildenafil citrate

**Start Date:**  
7/23/2002

**Est. Completion Date:**  
Aug 03

**Periodic Review:**

**Study Objective:** To continue to assess change in self-esteem and overall relationships for a period of 9 months in men with erectile dysfunction who are treated with open-label Viagra (sildenafil citrate) and who participated in a recently completed double-blind Viagra study.

**Technical Approach:** This study will look at males 18 years of age and older with documented erectile dysfunction for 9 months who have completed the double-blind Viagra (sildenafil citrate) study, A1481118. Approximately eight patients will be enrolled here at MAMC. This is a 9 month study and will include 7 visits to be completed at visit 1/week 0, visit 2/week 2, visit 3/week 6, visit 4/week 14, visit 5/week 22, visit 6/week 30, and visit 7/week 36. The first visit will be conducted on the same day as the last visit of the double-blind A1481118 study as applicable. Visit 1/week 0 procedures: Before any study procedures are conducted the patient will read the informed consent, and all questions and concerns will be answered by the primary investigator. After signing the informed consent the patient will then be given a copy to keep. The patient will then be given the same randomization number as in the previous study. The inclusion/exclusion criteria will be reviewed. Viagra will be dispensed to the patient along with Dosing Log Worksheets and Subject Instructions for Taking Study Medication. Instructions will also be provided verbally to the patient. If the subject does not meet the inclusion/exclusion criteria he will be discontinued from the study and followed by standard of care. The study staff will complete the screening failure page. At this visit all patients will start with a dose of 50 mg Viagra. Visit 2 (week 2): At this visit, concomitant drug treatment and concomitant non-drug treatment will be recorded, as well as any adverse events. We will review the Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. Sitting and standing blood pressure measurements and heart rate will be recorded, and new event log worksheets will be dispensed. The patient will be dispensed sufficient medication for the next four weeks, given Dosing Log Worksheets and appropriate dosing instructions. If a patient is discontinued from the study at this visit the Final/Premature Termination visit (visit 7/week 36) will be completed. Visit 3 (week 6): At this visit we will review the Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. Concomitant drug treatment and concomitant non-drug treatment will be recorded, as well as any adverse events. Drug accountability will be checked, and any patient that fails to satisfactorily account for any missing study medication after being counseled once should not be permitted to continue in the study. The therapeutic response will be assessed to determine if dosage requires adjustment. Sitting and standing blood pressure measurements and heart rate will be recorded, and new Dosing Log Worksheets will be dispensed. Enough study medication for the next 8 weeks will be dispensed until the next visit with dosing instructions. If a patient is discontinued from the study at this visit the Final/Premature Termination visit (visit 7/week 36) will be completed. Visit 4 (week 14): For this visit, drug accountability will be checked, and any patient that fails to satisfactorily account for any missing study medication after being counseled once should not be permitted to continue in the study. Concomitant drug treatment and concomitant non-drug

treatment will be recorded, as well as any adverse events. We will review Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. The therapeutic response will be assessed to determine if dosage requires adjustment. Sitting and standing blood pressure measurements and heart rate will be recorded, and new Dosing Log Worksheets will be dispensed. The patient will complete the Self-Esteem/Overall Relationship Questionnaire and the IIEF (International Index of Erectile Function). Enough study medication for the next 8 weeks will be dispensed with dosing instructions. If a patient is discontinued from the study at this visit the Final/Premature Termination visit (visit 7/week 36) will be completed. Visit 5 (week 22): At this visit we will review the Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. Concomitant drug treatment and concomitant non-drug treatment will be recorded, as well as any adverse events. Drug accountability will be checked, and any patient that fails to satisfactorily account for any missing study medication after being counseled once should not be permitted to continue in the study. The therapeutic response will be assessed to determine if dosage requires adjustment. Sitting and standing blood pressure measurements and heart rate will be recorded, and new Dosing Log Worksheets will be dispensed. Enough study medication for the next 8 weeks will be dispensed with dosing instructions. If a patient is discontinued from the study at this visit the Final/Premature Termination visit (visit 7/week 36) will be completed. Visit 6 (week 30): At this visit we will review the Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. Concomitant drug treatment and concomitant non-drug treatment will be recorded, as well as any adverse events. Drug accountability will be checked, and any patient who fails to satisfactorily account for any missing study medication should not be permitted to continue in the study. Sitting and standing blood pressure measurements and heart rate will be recorded. Enough study medication for the next 6 weeks will be dispensed with dosing instructions. If a patient is discontinued from the study at this visit the Final/Premature Termination visit (visit 7/week 36) will be completed. Visit 7 (week 36): At this final visit we will review the Dosing Log Worksheets and attempt to clarify reasons for any missing or ambiguous data. Concomitant drug treatment and concomitant non-drug treatment will be recorded, as well as any adverse events. Drug accountability will be checked. Sitting and standing blood pressure measurements and heart rate will be recorded. The subject summary will be completed. The patient will complete the Self-Esteem/Overall Relationship Questionnaire and the IIEF (International Index of Erectile Function). The outcome variables for this study are the change from baseline in the Self-Esteem Domain of the Self-esteem/Overall Relationship Questionnaire. This will be analyzed by comparing the patient answers on questions of the questionnaire from baseline until the final visit.

**Progress:** One patient enrolled in this study at MAMC during FY02. Patients are pending enrollment. Follow-up will continue.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/097 | <b>Status:</b> Ongoing |
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**Title:** A Multicenter, Phase IIb, Four Arm, Dose Finding, Randomized, Placebo-Controlled Study to Determine the Long Term Prostate Cancer Chemoprevention Efficacy and Safety of 20 mg, 40 mg, & 60 mg Daily of GTx-006 in Men with High Grade Prostate Intraepithelial Neoplasia (PIN)

**Principal Investigator:** COL Raymond A. Costabile, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Robert C. Allen, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Kevin J. Chismire, MC; COL Elizabeth A. Hansen, MC; LTC Roger K. George, MC

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**Keywords:** Prostate Intraepithelial Neoplasia (PIN), Prostate Cancer, Transrectal Ultrasound (TRUS), Digital Rectal Examination (DRE)

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**Start Date:**

5/22/2001

**Est. Completion Date:**

Oct 02

**Periodic Review:**

4/23/2002

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**Study Objective:** Primary: 1) To determine whether GTx-006 is able to reduce the incidence of prostate cancer in men with high grade PIN; 2) To evaluate the safety of GTx-006 (general, ocular, hormonal, semen profile and liver toxicities); 3) To determine the effective dose of GTx-006. Secondary: 1) To determine whether GTx-006 is able to eliminate or reduce high grade PIN lesions; 2) To test the effects of GTx-006 on serum total and % free PSA levels; 3) To assess the population; 4) pharmacokinetics of GTx-006; 5) To investigate whether GTx-006 affects prostate volume; 6) To assess the effects off GTx-006 on low grade PIN; 7) To assess quality of life issues.

**Technical Approach:** This phase IIb, multicenter, double-blind, placebo-controlled study will be looking at the efficacy and safety of GTx-006 in men with high grade prostate intraepithelial neoplasia (PIN). Eligible subjects will receive GTx-006 or identical appearing placebo for maximum treatment duration of 12 months. A total of 500 subjects will be enrolled across the United States (125 in each arm), with 120 subjects being enrolled into a semen sub-set (30 in each arm) that will look at sperm count. Inclusion criteria includes: diagnosis of high grade PIN (grade II or III) on prostate biopsy, PSA of 12 ng/ml, and adequate bone marrow, liver and renal function. Exclusion criteria includes: prior chemoprevention therapy, diagnosis of prostate cancer on initial evaluation or history of other cancer, visual acuity of 6/12 or worse, active eye disease or intraocular surgery, any infection requiring treatment, severe concurrent illness judged by the investigator as causing difficulty with adequate follow-up/compliance, thromboembolic disease, chronic hepatitis/cirrhosis, or subject taking any of the following medications: finasteride or testosterone-like supplements, such as DHEA (Dehydroepiandrosterone), herbal medications or dietary supplements for prostate health such as PC-SPEs and Saw Palmetto. Subject may wash-out of excluded medications for 30 days and then be eligible for study as long as he agrees not to re-start medication while on study. Before performing any study related procedures, the study coordinator or investigator will explain the purpose of the study to the patient, the study procedures and the study schedule. After giving the patient a chance to ask questions, the coordinator will have the patient read and sign the informed consent. Then a member of the study staff will obtain a medical history, history of prior medications within 30 days, & vital signs. Blood and urine specimens will be sent to a central laboratory. An investigator will give a complete physical examination, including Digital Rectal Examination (DRE). A Transrectal Ultrasound (TRUS) and prostate biopsy will be done if none done within 6 months. A pathologist from a central laboratory will confirm the results of the biopsy prior to randomization. In addition, an ophthalmic examination will be done. Upon determining that the patient qualifies after review of all tests, inclusion/exclusion criteria and examinations, then the patient will be randomized within 30 days of the screening visit. He will be given a subject number and randomized to one of 4 treatment arms - 20 mg, 40 mg, 60 mg or placebo. To randomize the patient, the coordinator will

use the next sequential randomization number from the block of study drug supplied by the study sponsor. Also, at the randomization visit the following procedures/assessments will occur: check for concomitant medications and symptoms of illness/injury, obtain vital signs, do semen analysis - sperm count (subset of subjects from selected sites), administer Quality of Life Questionnaire (QOL), obtain lab specimens, and dispense daily diary instructing patient how to complete drug intake information. The study drug will be started in the clinic during this visit. The study staff will then contact the patient by telephone within seven (7) days to assess study drug compliance and tolerance. The patient will return at 3 months, 6 months, 9 months, and 12 months after randomization. The procedures/assessments will be the same as at the randomization visit with the addition of the following: drug accountability at each visit, physical examination at each visit including DRE, urinalysis at each visit, Semen analysis at Months 6 & 12, TRUS for volumetric measurement of prostate at months 6 & 12, prostate biopsy at Months 6 & 12, and ophthalmic examination at Month 12. In the event that the patient discontinues prematurely from the study, he will be asked to return to the site as soon as possible to have the 12-Month assessments/procedures performed, regardless of the study day.

**Progress:** During FY02, a total of 6 patients have been enrolled into this study here at MAMC. 3 patients have received study treatment, 2 are still in screening and 1 patient was a screen failure. This study is still open to enrollment and patient follow-up will continue for FY02.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/064 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Multicenter, Randomized, Parallel Group, Double-Blind, Placebo Controlled, Flexible Dose Escalation Study to Evaluate Self-Esteem and Overall Relationships in Men with Erectile Dysfunction Treated with Viagra (sildenafil citrate) in the United States

**Principal Investigator:** COL Raymond A. Costabile, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Robert C. Allen, MC; LTC Henry E. Ruiz, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Leah P. McMann, MC; MAJ Thomas L. Poulton, MC

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**Keywords:** self esteem sildenafil viagra quality of life QOL erectile dysfunction ED, military specific

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**Start Date:**  
4/23/2002

**Est. Completion Date:**  
May 03

**Periodic Review:**

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**Study Objective:** To assess change in self esteem and overall relationships in men with erectile dysfunction who are treated with Viagra To correlate the self-esteem and overall relationship measures with efficacy measures.

**Technical Approach:** This study will look at males, 18 years of age and older, with documented erectile dysfunction. They must have a partner for the duration of the study and be Viagra naive. Approximately eight patients will be enrolled here at MAMC. This is a 14 week study, commencing with a 2-week screening phase followed by a 12 week treatment phase. Before any study procedures are conducted, the patient will read the informed consent and all questions and concerns will be answered by the primary investigator. The patient will be given a screening number and the SHI-M questionnaire to confirm the diagnosis of ED, and the Self-Esteem/Overall Relationship Questionnaire to complete. Throughout the course of the study the patient will be asked about concomitant and non-concomitant drug treatment, an event log will be dispensed and instructions for completing it will be given. Serious Adverse Events, questionnaires from both partners will be evaluated and noted. The outcome variables for this study are the change from baseline in the Self-Esteem domain of the Self-Esteem/Overall Relationship Questionnaire. This will be analyzed by comparing the patient answers on questions 9-12 of the questionnaire from baseline until the final visit.

**Progress:** A total of 10 patients have been enrolled in this study at MAMC during FY02. One patient was a screen failure and one patient withdrew consent. Two patients withdrew early due to lack of efficacy. One patient has completed treatment and five remain in follow-up. Follow-up will continue for FY03.



### Detail Summary Sheet

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|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/050                 | <b>Status:</b> Terminated             |
| <b>Title:</b> A Multicenter, Randomized Phase III Study of Adjuvant Oncophage Versus Observation in Patients with High Risk of Recurrence After Surgical Treatment for Renal Cell Carcinoma |  |                                       |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC   |  |                                       |
| <b>Department:</b> Surgery/Urology  |  | <b>Facility:</b> MAMC                 |
| <b>Associate Investigator(s):</b> MAJ Raymond S. Lance, MC  |  |                                       |
| <b>Keywords:</b> Oncophage carcinoma recurrence, renal cell carcinoma, cancer, observation  |  |                                       |
| <b>Start Date:</b><br>1/23/2001   | <b>Est. Completion Date:</b><br>Feb 03 | <b>Periodic Review:</b><br>12/19/2001 |

**Study Objective:** The primary objective of the study is to ascertain whether patients randomized to receive Oncophage® treatment for surgically resected, locally advanced renal cell carcinoma have a statistically longer survival than patients with no adjuvant treatment. The secondary objectives of the study are (1) To ascertain whether patients randomized to Oncophage® have a statistically longer progression-free survival than patients with no adjuvant treatment and (2) To further characterize the safety of treatment with Oncophage®.

**Technical Approach:** This is an international, multi-center, randomized, open-label Phase III study in which patients with surgically resected, locally advanced renal cell carcinoma at high risk of recurrence will be randomized post-operatively to receive adjuvant treatment with Oncophage or no adjuvant treatment (observation, standard of care). Approximately 850 patients will be enrolled internationally over a period of two years to obtain 712 evaluable patients for overall survival and progression free survival in this trial. At least 12 patients will be enrolled at Madigan Army Medical Center.

Prior to surgery and after informed consent is obtained, patients will be screened for study and inclusion/exclusion criteria will be reviewed. Vital signs, performance status, and laboratory tests will be performed including proof of non-pregnancy. Other appropriate studies to fully define the extent of existing or suspected malignant and non-malignant disease will be done including CT-chest, CT or MRI of abdomen/pelvis, and CT or MRI of the brain. A bone scan will be performed if clinically indicated. All patients will undergo complete surgical resection of their tumors, and will be randomized to receive adjuvant treatment with Oncophage or to receive no adjuvant treatment. Patients will be stratified for histological grade, nodal status, and performance status. The major part of the patient's tumor will be sent to Antigenics for preparation of Oncophage, which is an autologous tumor-derived vaccine. Patients randomized to Oncophage treatment will receive the first four injections at weekly intervals and thereafter at two-week intervals, until possible disease progression, excessive toxicity, or the patient's available supply of Oncophage is depleted. Patients will receive a ruler and diary and asked to record possible reactions to the vaccine which may occur at home. Patients on both arms will be assessed for adverse events, vital signs, performance status, lab tests, x-rays, safety and efficacy at 1-3 month intervals for the first year. All patients will undergo x-rays every 3 months for first year. Thereafter, they will be evaluated every 6 months for possible progressive disease until death. Auto-antibodies will be monitored every 6 months for the first year for patients receiving Oncophage and once every year for patients on the observation arm.

**Progress:** This protocol closed to enrollment at MAMC, effective Jan 02, per the study sponsor. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/113 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

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**Title:** A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer (M00-258)

**Principal Investigator:** COL Raymond A. Costabile, MC

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|------------------------------------|-----------------------|
| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Robert C. Allen, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC; MAJ Thomas L. Poulton, MC; CPT Jack R. Walter, MC

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**Keywords:** angiotensin-converting enzyme (ACE), prostate specific antigen (PSA), P-glycoprotein (PGP)

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**Start Date:**  
6/26/2001

**Est. Completion Date:**  
Jul 02

**Periodic Review:**  
5/14/2002

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**Study Objective:** To evaluate the safety of 10 mg Atrasentan for the treatment of prostate cancer. In addition, the pharmacokinetic parameters of Atrasentan will be defined in a sub-population of subjects.

**Technical Approach:** This is a phase III, open label study evaluating the safety of 10 mg Atrasentan in men with hormone refractory prostate cancer. All men enrolled in this protocol must have successfully met all of the eligibility criteria for this trial and have completed one of the following Phase III trials:

M00-211: A Phase III, Randomized, Double-Blind, Placebo controlled Study Evaluating the Safety and Efficacy on 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer  
M00-244: A Phase III, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic Hormone Refractory Prostate Cancer  
Eligible men will receive a single, oral dose (soft gelatin capsule) of 10 mg atrasentan before leaving the clinic (Day 1). They will then continue taking the same dose of study drug once a day at approximately the same time each day. The study participants will be asked to return to the clinic on study days 14 & 28, at Week 12, and then every 12 weeks thereafter. Upon study completion the participants will be asked to come into the clinic for a final assessment, and will return again for a safety evaluation 30 days after the last dose of study drug. Blood will be drawn at every visit. Urine samples will be obtained at visit Day 1, Day 28, every 12 weeks and at final visit.

**Progress:** A total of 4 patients have been enrolled into this study at MAMC during FY02. All four patients have received study drug. All four patients remain active in the study and continue to be followed. This study is still open to enrollment.

## Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 201/107                 |  | <b>Status:</b> Ongoing               |  |
| <b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)   |  |  |  |                                      |  |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC   |  |  |  |                                      |  |
| <b>Department:</b> Surgery/Urology  |  |  |  | <b>Facility:</b> MAMC                |  |
| <b>Associate Investigator(s):</b> LTC Robert C. Allen, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC; MAJ Thomas L. Poulton, MC; CPT Jack R. Walter, MC   |  |  |  |                                      |  |
| <b>Keywords:</b> angiotensin-converting enzyme (ACE), prostate specific antigen (PSA), prostate cancer (PCa), P-glycoprotein (PGP) transporter, cytochrome P-450 3A4 (CYP3A4)   |  |  |  |                                      |  |
| <b>Start Date:</b><br>6/26/2001   |  | <b>Est. Completion Date:</b><br>Jul 02 |  | <b>Periodic Review:</b><br>6/25/2002 |  |
| <b>Study Objective:</b> Primary: To evaluate the safety and efficacy as measured by time-to-disease progression. Secondary: To evaluate the effect of 10 mg Astrasentan on: PSA progression, Biochemical bone markers, Bone scan index, Survival and to evaluate the effect of the study drug on quality of life and performance status and to perform population pharmacokinetic analysis.   |  |  |  |                                      |  |
| <b>Technical Approach:</b> This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last £ 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. The patient will be randomized in a 1:1 ratio to receive either atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Neither the investigator nor the patient will know which arm the patient is on. Participants will be assigned a 4-digit study number and will be given study drug prior to leaving the clinic. Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. Participants will visit the clinic on Day 14, Weeks 4, 8, & 12, and every 6 weeks thereafter. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. In addition, at each visit the patient will receive a physical examination, & will have vital signs taken. Atrasentan trough plasma concentrations will be measured at Week 4 & Week 12 only. Laboratory analyses (chemistry, hematology, etc.) will be performed at a central laboratory. Quality of Life (QOL) assessment questionnaires will be completed at Day 1, Week 4, Week 12 and every 12 weeks thereafter. The QOL questionnaire will also be completed at final visit and 30 days later. A diary will be given to the patient to collect a record of medication taken for pain. The diary will be reviewed at each visit. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends (as defined by when 650 subjects have experienced confirmed events of disease progression). The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above. |  |  |  |                                      |  |
| <b>Progress:</b> A total of 8 patients have been enrolled in this study at MAMC during FY02. Three patients were screen failures, 5 patients received study treatment. Four patients completed, and one patient remains active. Patient follow-up will continue FY03.   |  |  |  |                                      |  |

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/121      **Status:** Ongoing

**Title:** A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)

**Principal Investigator:** COL Raymond A. Costabile, MC

**Department:** Surgery/Urology      **Facility:** MAMC

**Associate Investigator(s):** LTC Robert C. Allen, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC; MAJ Thomas L. Poulton, MC; CPT Jack R. Walter, MC

**Keywords:** angiotensin-converting enzyme (ACE), prostate specific antigen (PSA), prostate cancer (PCa), P-glycoprotein (PGP) transporter, cytochrome P-450 3A4 (CYP3A4)

**Start Date:**  
7/24/2001

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
8/27/2002

**Study Objective:** Primary: To evaluate the safety and efficacy as measured by time-to-disease progression. Secondary: (1) To evaluate the effect of 10 mg Astrasentan on: PSA progression, Biochemical bone markers, Bone scan index, (2) Survival, (3) To evaluate the effect of the study drug on quality of life and performance status and (4) To perform population pharmacokinetic analysis.

**Technical Approach:** This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. Informed consent will be obtained by one of the investigators or by one of the study coordinators. The patient will then enter the screening phase, which will last less than or equal to 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. After the patient has met eligibility criteria, the patient will be randomized in a 1:1 ratio to receive either atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. In addition, at each visit the patient will receive a physical examination, & will have vital signs taken. Atrasentan trough plasma concentrations will be measured at Week 4 & Week 12 only. Laboratory analyses (chemistry, hematology, etc.) will be performed at a central laboratory. Quality of Life (QOL) assessment questionnaires will be completed at Day 1, Week 4, Week 12 and every 12 weeks thereafter. The QOL questionnaire will also be completed at final visit and 30 days later. A diary will be given to the patient to collect a record of medication taken for pain. The diary will be reviewed at each visit. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends. The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

**Progress:** A total of 7 patients were enrolled in this study here at MAMC during FY02. Five patients received study treatment, one patient withdrew consent before receiving study drug and one patient withdrew consent after receiving study drug. One patient was a screen failure. Four patients remain in follow-up and this study is still open to enrollment.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 200/112                 | <b>Status:</b> Ongoing               |
| <b>Title:</b> A Phase III, Randomized, Multicenter, Placebo-controlled, Double-blind, Clinical Trial to Study the Efficacy and Safety of CyPat (Cyproterone Acetate [CA]) for the Treatment of Hot Flashes Following Surgical or Chemical Castration of Prostate Cancer Patients and Its Impact on the Quality of Life in these Patients   |  |                                      |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC  |  |                                      |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC   |  |                                      |
| <b>Keywords:</b> hot flashes, surgical castration, chemical castration, prostate cancer, placebo, CyPat, Cyproterone Acetate (CA)  |  |                                      |
| <b>Start Date:</b><br>7/25/2000  | <b>Est. Completion Date:</b><br>Sep 01 | <b>Periodic Review:</b><br>6/25/2002 |
| <b>Study Objective:</b> 1) To determine the efficacy of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or “medical castration”(LHRH agonist treatment); 2) To compare the effectiveness of the two doses (50 and 100mg) of CyPat for control of hot flashes; 3) To determine safety (based on adverse events and laboratory parameters) of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or “medical castration”(LHRH agonist treatment); 4) To determine the impact of CyPat treatment on the quality of life in surgically or chemically treated cancer patients. |  |                                      |
| <b>Technical Approach:</b> After a one-week screening observation period, subjects will be randomized to receive either placebo, 50mg, or 100 mg of CyPat to control hot flashes. For 12 weeks, subjects will record incidence of hot flashes, and will periodically have checkups to ensure patient safety. Patients will complete quality of life questionnaires on a monthly basis during the treatment phase of this study. After the 12-week double-blind randomized part, eligible patients will have the option of continuing to take CyPat (100mg) for 6-9 months in an open label tolerability study.   |  |                                      |
| <b>Progress:</b> A total of 19 patients have been enrolled in this study at MAMC, with 5 patients enrolled during FY02. Thirteen patients have received study treatment, 4 patients were screen failures. Eight patients withdrew consent, one before receiving study drug and 7 after receiving study drug. 2 patients were discontinued. 5 patients are still in follow-up. Study is still open to enrollment and patient follow-up will continue for FY02.  |  |                                      |

### Detail Summary Sheet

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|--|--|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02   |  | <b>Number:</b> 200/019                 | <b>Status:</b> Completed              |
| <b>Title:</b> A Pilot Study of Radiofrequency Induced Coagulation Necrosis of Solid Renal Masses |  |  |                                       |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC                                      |  |  |                                       |
| <b>Department:</b> Surgery/Urology   |  | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ David G. Omdal, MC   |  |  |                                       |
| <b>Keywords:</b> cancer, radiofrequency ablation, kidney, tumor                                  |  |  |                                       |
| <b>Start Date:</b><br>11/19/1999   |  | <b>Est. Completion Date:</b><br>Dec 04 | <b>Periodic Review:</b><br>10/24/2000 |

**Study Objective:** (1)To assess the capability of radiofrequency (RF) energy to induce a predictable zone of necrosis within renal tissue / tumor, (2) to determine the viability of cells within the zone of necrosis via pathological evaluation and (3) to evaluate the response and follow up in patients who are not candidates for surgical resection of their solid renal masses.

**Technical Approach:** This prospective, nonrandomized study will treat various stages of renal cell cancer using radiofrequency (RF) induced necrosis of tumor tissue. The investigator will use ultrasound imaging to place an electrode into the affected tissue. The appropriate dose of RF energy will be released into the tissue in the immediate area. If the patient is a candidate for resection nephrectomy, the treated tissue will then be resected and assessed by pathological evaluation. After treatment, both groups will be followed and monitored to assess changes in the tumor and surrounding tissue.

**Progress:** A total of 14 patients enrolled in this study at MAMC, 8 in the ablation only arm and 6 in the ablate and resect arm. Six patients in the ablation only arm show no evidence of progression and two have had progression of their renal carcinoma with subsequent additional therapy. Pathological data has shown tumor ablation in all evaluable specimens and two with tissue necrosis. All study related interventions are completed. Study data collection is complete.

## Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/095                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Placebo-Controlled, Double-Blind, Randomized, Parallel Study of the Efficacy and Safety of Dapoxetine HCI in the Treatment of Rapid Ejaculation, Protocol Number C-2002-012-00   |  |                         |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC  |  |                         |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> LTC Robert C. Allen, MC; MAJ Raymond S. Lance, MC  |  |                         |
| <b>Keywords:</b> Golombok Rust Inventory of Sexual Satisfaction Intravaginal Ejaculatory Latency Time Rapid Dapoxetine   |  |                         |
| <b>Start Date:</b><br>7/23/2002  | <b>Est. Completion Date:</b><br>Oct 03 | <b>Periodic Review:</b> |
| <p><b>Study Objective:</b> The objectives of this study are to determine the efficacy and safety of two dosage strengths of dapoxetine HCI (30 mg and 60 mg) in males with rapid ejaculation and to characterize the population pharmacokinetics of dapoxetine in males with rapid ejaculation</p> <p><b>Technical Approach:</b> This study will be looking at males 18 years of age and older with Intravaginal Ejaculatory Latency Time (IELT)of = 2 minutes . Approximately 20-30 patients will be enrolled in this protocol here at MAMC. Study subject's partners will also be asked to complete informed consent. Patients will attend the clinic on 5 occasions: at screening (Visit 1), End of Baseline/Randomization (Visit 2), Week 4 (Visit 3), Week 8 (Visit 4) and at Week 12 Final (Visit 5). If a discontinuation of medication is necessary the patient and his partner must return to complete the Screening Visit after the appropriate washout interval is complete. At the screening visit the Inclusion /Exclusion criteria will be reviewed and the patient will have a physical exam (including vital signs), EKG, review medical history, blood will be drawn for laboratory testing, concomitant medications will be recorded, baseline questions and the GRISS Questionnaire will be completed. The partner will undergo a pregnancy test, baseline questions and the GRISS Questionnaire will be completed. The partner will be given a packet containing the Baseline Questions with instructions to complete the questions at the end of the 2-week Baseline period and mail then to the study coordinator. Both the patient and his partner will be given an Event Log and stopwatch for recording IELT and instructions for their use. At this visit the patient and his partner will receive instructions regarding the use of the study medication and sexual intercourse and be advised that strict adherence to these instructions are required. Visit 2-End of Baseline/Randomization, the patient will return to the clinic with the completed Baseline Event Log. At this visit vital signs will be checked, concomitant medications recorded, AE's recorded, completion of Baseline Questions checked, eligibility for Randomization reviewed, and if randomized a blood sample obtained for metabolic genotyping of cytochrome P450 isozymes. If the patient continues to meet all of the eligibility criteria he will be randomized to receive a drug kit number. A Treatment Event log and study medication (30 doses for the next 4 week period) will be dispensed, as well as a packet for his partner containing Follow-Up Questions to be completed at the end of the 4 week treatment period and mailed to the study coordinator. The instructions for the use of study medication and sexual intercourse that were given at Visit 1 will be repeated. PK Sites: After completing Visit 2 randomization procedures, the patient will be given one dose of study drug while in the clinic, which will be removed from the patient's assigned study medication blister pack by the study coordinator. The date and time of this dose will be recorded on the CRF by the study coordinator. The remainder of the blister packs will be kept at the site until the patient completes the PK procedures. Three blood samples for PK analyses will be drawn at the following intervals: sample 1 will be drawn day of dosing 30 minutes-2 hours after dose has been given, sample 2 will be drawn day of dosing 4-8 hours after dose has been given and sample 3 will be drawn the day after dosing 24-32 hours after dose has been given. After the third sample has</p> |  |                         |

been drawn the patient will be given the remaining 29 doses of study medication for the next 4 weeks, along with a Treatment Event Log and a packet for his partner containing Follow-Up Questions to be completed at the end of the 4 week treatment period and mailed to the study coordinator. Visit 3-Week 4 and Visit 4-Week 8: The patient will return to the clinic with the study medication blister packs and Event Log and the following procedures performed: completed Treatment Event Log collected and reviewed, vital signs checked, concomitant medications recorded, AE's recorded, Completion of Follow-up questions. The patient will be given a new Treatment Event Log, a supply of study drug (30 doses for the next 4 weeks) and a packet for his partner containing Follow-Up Questions to be completed at the end of the 4 week treatment period and mailed to the study coordinator. Visit 5, Week 12-Final Clinic Visit: At this visit the patient will return to the clinic with the study medication blister packs and Event Log and the following procedures will be performed, completed Treatment Event Log collected and reviewed, vital signs checked, physical exam, EKG, blood will be drawn for laboratory testing, concomitant medications recorded, AE's recorded, Completion of Follow-up questions.

**Progress:** This study has not yet begun here at MAMC due to sponsor hold and a pending amendment.



### Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/008

**Status:** Ongoing

**Title:** A Placebo-controlled Study of Cystistat (Sodium Hyaluronate) for the Treatment of Interstitial Cystitis

**Principal Investigator:** COL Raymond A. Costabile, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, MC; LTC Henry E. Ruiz, MC; MAJ Andrew C. Peterson, MC; CPT Leah P. McMann, MC

**Keywords:** IC; Interstitial Cystitis

**Start Date:**

10/23/2001

**Est. Completion Date:**

Jan 03

**Periodic Review:**

**Study Objective:** To evaluate the safety and efficacy of Cystistat compared to placebo in reducing three symptoms associated with interstitial cystitis.

**Technical Approach:** This will be a multi-center, randomized, double-blind, placebo-controlled study designed to assess the safety and efficacy of intravesical sodium hyaluronate (Cystistat) compared to placebo in the treatment of interstitial cystitis (IC). One hundred and twenty-two (122) patients, approximately 61 patients in each arm, will be treated at fourteen to eighteen sites in the U.S. and Canada. Patients diagnosed with interstitial cystitis are eligible for the study. A cystoscopic examination will have been performed within one year of study entry (bladder biopsies only if carcinoma suspected) and patients will meet the required baseline symptom scores. In addition, eligible patients will have a sterile bacterial urine culture. Consented patients will be randomized in a 1:1 ratio to active treatment (Cystistat: 40 mg sodium hyaluronate in phosphate buffered saline to give a total volume of 50 mL) or placebo (50 mL phosphate buffered saline) and will be treated once a week for six weeks. Patients will receive the same therapy (either Cystistat or placebo) in each of the six treatment visits. Cystistat or placebo will be instilled into the bladder by catheter, the catheter will be removed and the solution will be held in the bladder for a period of time ranging from 30 min to 2 hours, after which time the solution will be voided. The efficacy of Cystistat in the treatment of IC will be assessed at Week 8 by evaluating Pain (VAS 10 cm) and Overall Change in Condition (Patient Global Assessment). In addition, secondary endpoints assessed: Urgency (VAS 10 cm), Urinary Frequency (Voiding Log), Symptom/Problem Index, Quality of Life Questionnaire (SF-36), and Sexual Function Assessment (VAS 10 cm). Efficacy measurements (Pain VAS, Urgency VAS, Voiding Log) will be obtained using patient diaries prior to the first treatment and weekly thereafter up to and including Week 8. The Symptom/Problem Index, Quality of Life Questionnaire and Sexual Function Assessment will be completed prior to the first treatment and again at Weeks 4 and 8. The Patient Global Assessment will be completed at Week 8. In addition, Pain and Urgency (10 cm VAS), Symptom/Problem Index, Quality of Life Questionnaire, Sexual Function Assessment, and the Patient Global Assessment will be completed at Weeks 12 and 16 to assess any sustained effect from the study therapy.

**Progress:** A total of 7 patients enrolled in this study at MAMC during FY02. Seven patients received study treatment, five have completed the study with 2 patients remaining for follow-up. Enrollment has closed for this study. No SAE's noted during this study either MAMC or NON-MAMC. Patients follow-up continued during FY02.

### Detail Summary Sheet

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|------------------------|-----------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/090 | <b>Status:</b> Terminated |
|------------------------|-----------------------|---------------------------|

**Title:** A Randomized Double-Blind Placebo-Controlled Phase III Trial Evaluating Zoledronate Plus Standard Therapy versus Placebo Plus Standard Therapy in Patients with Recurrent Carcinoma of the Prostate Who Are Asymptomatic with Castrate Levels of Testosterone and Have Rising PSA Levels Without Radiologically-evident Metastatic Disease

**Principal Investigator:** COL Raymond A. Costabile, MC

|                                    |                       |
|------------------------------------|-----------------------|
| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
|------------------------------------|-----------------------|

**Associate Investigator(s):** MAJ Bryon D. Joyner, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C. Evans, MC; MAJ Andrew C. Peterson, MC; LTC Henry E. Ruiz, MC; MAJ David E. McCune, MC

**Keywords:** Cancer: prostate, recurrent carcinoma, Zoledronate

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Oct 05

**Periodic Review:**  
6/25/2002

**Study Objective:** To determine if intravenous infusions with 8mg zoledronate is superior to placebo in the prevention of bone metastases.

**Technical Approach:** This is a prospective, stratified, randomized, double blind, placebo-controlled multicenter study in parallel groups. Five hundred prostate cancer patients with castrate levels of testosterone who are progressing biochemically by PSA only and have no radiologically evident metastases will be enrolled. Patients will be stratified according to the prior local treatment and the time interval between surgical castration or initiation of LHRH agonist and trial entry. Patients will receive double-blind study treatment until the development of bone metastases. After the development of bone metastases, all patients will receive open-label 8 mg zoledronate until the end of the study. Both the double-blind treatment phase and the open-label treatment phase have a fixed assessment schedule that must be followed. Once patients have completed the 48th month of the fixed assessment schedule, all patients will be followed for survival until LPLV (Last Patient Last Visit). LPLV for this study is defined as the time when the last patient completes the 4th month of study visit or has died. Assuming a placebo bone metastases-free survival rate of 20% at 2 years, this study is powered to determine if sequential infusion with 8 mg zoledronate administered every 4 weeks is superior to placebo in increasing the bone metastases- survival rate at 2 years to 32% (reduction of the hazard rate of bone metastatic disease in patients with prostate cancer by 29%). It is planned that the data from all centers that participate in this protocol will be combined, so that an adequate number of patients will be available for analysis. The Biostatistics department of Novartis will analyze the data from this study.

**Progress:** This study has been terminated by the sponsor. No further patient follow-up is required. A total of 11 patients enrolled in this study at MAMC. 4 patients received study treatment, 5 patients withdrew consent , one before receiving study drug and four after receiving study drug. There were 6 screen failures. One patient died while in follow-up but was no longer taking study drug. This death was considered unrelated to study participation and a normal progression of disease.

### Detail Summary Sheet

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|---|--|--------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 200/141                 | <b>Status:</b> Terminated            |
| <b>Title:</b> A Study Evaluating the Efficacy, Safety, and Tolerability of L-377202 in Bidimensionally Measurable, Androgen-Independent Prostate Cancer (Protocol No. 004-00) |  |                                      |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC   |  |                                      |
| <b>Department:</b> Surgery/Urology  |  | <b>Facility:</b> MAMC                |
| <b>Associate Investigator(s):</b> MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; LTC Henry E. Ruiz, MC; MAJ Nancy Shaffer, MC  |  |                                      |
| <b>Keywords:</b> L-377202, prostate cancer, androgen-independent prostate cancer  |  |                                      |
| <b>Start Date:</b><br>9/26/2000   | <b>Est. Completion Date:</b><br>Dec 02 | <b>Periodic Review:</b><br>8/22/2002 |

**Study Objective:** The primary objectives of this study are to determine bidimensionally measurable disease radiologic response rates after treatment with L-377202 and to evaluate the general safety and tolerability of L-377202. The secondary objectives are (1) to determine bidimensionally measurable disease response rates (tumor burden, bone scan), (2) to evaluate PSA response rates obtained, (3) to evaluate pain and analgesic response rates, (4) to evaluate health-related quality-of-life responses, (5) to determine time to response, time to progression and response duration, (6) to determine duration of time during which patients maintain an ECOG performance status  $\leq 1$ , (7) evaluate 1 year cancer-specific and overall survival following treatment with L-333202, and (8) assess the effect of L-277202 treatment on biochemical markers of bone turnover.

**Technical Approach:** This is an open, nonrandomized study of male patients at least 30 years old with androgen-independent prostate cancer and bidimensionally measurable disease. After screening, eligible patients will be treated with a 30 minute infusion of L-377202, 225 mg/m<sup>2</sup> every 21 days. Each patient will be treated with at least 2 cycles, though additional cycles may be administered for stable or responding disease. Doses will be adjusted according to degree of myelosuppression experienced by each patient.

If a response or stabilization of disease is demonstrated, patients may continue to be treated for an indefinite number of cycles until either evidence of disease progression is documented, inclusion criteria can not be satisfied (except for PSA), or exclusion criteria are met. Assessments for disease progression must be performed every 2 treatment cycles. Pain will be assessed with the present pain intensity (PPI) scale of the McGill-Melzack Pain Questionnaire. Analgesic use will be assessed with the analgesic diary. Health-related quality-of-life will be assessed with the EORTC QLQ-C30 and the Osoba Quality-of-Life Module Prostate-14. The health economic impact of L-377202 will be assessed by collecting health resource utilization with the Health Economic Assessment case report form, which will be completed by the investigator or his designee. Duration of Time with an ECOG performance status  $\leq 1$  is defined as the number of days during which a performance status of  $\leq 1$  is reported.

**Progress:** This protocol closed to patient entry, 14 Jun 01, per the study sponsor. One patient was previously enrolled in this study at MAMC and continues to be followed by Urology Service.

## Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 201/090      **Status:** Ongoing

**Title:** A Two-Phase, Double-Blind, Randomized, Parallel-Group Design, Multicenter Study of FLOMAX® Capsules, 0.4 mg versus Placebo in Male Patients with Acute Urinary Retention Related to Benign Prostatic Hyperplasia

**Principal Investigator:** COL Raymond A. Costabile, MC

**Department:** Surgery/Urology      **Facility:** MAMC

**Associate Investigator(s):** MAJ Sunil K. Ahuja, MC; LTC Henry E. Ruiz, MC; LTC Robert C. Allen, MC; MAJ Raymond S. Lance, MC; MAJ Andrew C. Peterson, MC; MAJ Thomas L. Poulton, MC

**Keywords:** Acute urinary retention (AUR), benign prostatic hyperplasia (BPH), digital rectal examination (DRE), electrocardiogram (ECG), trial without catheter (TWOC)

**Start Date:**  
3/27/2001

**Est. Completion Date:**  
Apr 02

**Periodic Review:**  
3/26/2002

**Study Objective:** To establish whether the administration of FLOMAX® improves the outcome of a trial without catheter (TWOC) after an episode of acute urinary retention, and to determine whether spontaneous voiding is maintained over the course of six months of active treatment.

**Technical Approach:** This double-blind, placebo-controlled, randomized trial, is designed in two phases to examine whether FLOMAX® capsules, 0.4 mg as compared to placebo, can increase the success rate of TWOC in patients with acute urinary retention due to BPH (Phase I). The trial is powered to detect significant differences between FLOMAX® and placebo in Phase I. Phase II of the trial is designed to examine whether patients who successfully voided spontaneously in Phase I, can be maintained catheter free on treatment with FLOMAX® compared to placebo over a six-month period. The overall design of Phase II will examine whether FLOMAX® can prevent or delay reoccurrence of acute urinary retention due to BPH. Visit 1 may be performed after diagnosis of AUR and catheterization occur. If referred from the ER, Visit 1 must be performed within 72 hours of catheterization in order to be eligible for the study. Following obtaining of informed consent the study coordinator will review and record any relevant medical history for the last two years and review the inclusion/exclusion criteria for Phase I. Upon determining patient eligibility, the rest of Visit 1 procedures will be performed, sitting vital signs, physical examination, digital rectal examination, prostate volume, laboratory testing, concomitant therapy, and adverse events. The patient will then be randomized and a medication number will be assigned. The patient will be on study medication for 72-96 hours (3-4 days). The catheter must be in place during this treatment time. Patients will take the first dose of medication in the office the same day as Visit 1 and then 7 days of drug dispensed with instructions to take one capsule orally, one half-hour after breakfast for the next 3-4 days. If the dose is not taken one half-hour after breakfast, the patient will have up to three hours to take their dose. If the patient does not then take their medication within this three hour window the dose is considered missed. The patient should not double up doses at the next dosing time, instead only the next regular dose should be taken at the instructed time. Patients will be instructed to return to the clinic within 3-4 days (72-96 hours) after Visit 1. Visit 2 (day 3 or 4): At this visit, the patient's bladder will be filled with normal saline solution through the catheter to promote voiding. When the patient feels the sensation to urinate, the catheter will be removed and the patient instructed to spontaneously void. A successful spontaneous void is defined as a voided amount of at least 100ml and a post-void residual volume of equal to or greater than 300ml. Post-void residual volume will be measured, using ultrasound, for those patients that void spontaneously. These patients will be given the option of continuing in the Phase II portion of the study. Visit 2 is the final visit for patients who are unable to void spontaneously. These patients will not be allowed to continue to Phase II of the study and must be withdrawn. These patients will be re-catheterized and all Visit 2 procedures, as

checked in the flow chart including laboratory tests will be completed and all study medication will be returned. These patients will consult their own physicians for further treatment. Any patient who has removed his catheter or had it removed at another institution, should be discontinued and all end of study procedures performed. If the patients blood work from Visit 1 has clinically significant abnormal lab values, the patient should be withdrawn and all end of study procedures completed. Visit 2 procedures consist of physical examination, sitting vital signs, removing urethral catheter, laboratory tests (this test will only be completed for those patients not continuing on to the Phase II portion of the study), voided urine volume, post-residual volume (by pelvic ultrasound), medication compliance, adverse events, concomitant therapy, termination of trial medication for Phase I, study medication for the Phase II portion will be dispensed only if the patient is continuing on to the Phase II portion and meets all the inclusion/exclusion criteria.

Phase II inclusion criteria: Patients who have voided spontaneously at Visit 2, at least 100ml and a post-void residual volume of more than or equal to 300ml, at Visit 2. Patients will be re-randomized and a new medication number will be assigned. Patients will be dispensed a 90 day supply of medication and instructions to take their medication one half hour after breakfast. If the dose is not taken one half hour after breakfast, the patients will have up to three hours to take their dose. If the dose is missed the patient must not double up at the next dosing time. Instead only the next regular dose may be taken. These patients will be asked to return to the clinic 90 days from Visit 1. Visit 3 (90 days): This visit will collect the following information: sitting vital signs, medication compliance, adverse event and concomitant therapy. The patient will be ask to spontaneously void and voided urine will be collected and measured. A post-void residual measurement using pelvic ultrasound will also be done. A 90 day supply of medication will be dispensed and instructions to take their medication one half hour after breakfast. If the dose is not taken one half hour after breakfast, the patient will have up to three hours to take their dose. If the dose is missed the patient must not double up at the next dosing time. Instead only the next regular dose may be taken. These patients will be ask to return to the clinic 180 days after Visit 1. Visit 4 PEOT/EOT (180 days): This visit will collect the following information: physical examination, digital rectal exam, sitting vital signs, laboratory testing, voided urine volume, post-void residual volume (by pelvic ultrasound), prostate volume (by transrectal ultrasound), medication compliance, adverse events, concomitant therapy. The patient will also be ask to return all unused trial medication at this visit.

**Progress:** A total of 11 patients have been consented in this protocol at MAMC, with 7 enrolled during FY02. 11 patients have received Phase 1 study treatment, 6 patients have entered the Phase II portion w/ 2 completing treatment. The other 4 have been discontinued on study due to adverse events. Patient follow-up will be continued during FY03. One more patient remains to be enrolled.

### Detail Summary Sheet

**Date:** 30 Sep 02      **Number:** 96/158      **Status:** Ongoing

**Title:** Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis

**Principal Investigator:** COL Raymond A. Costabile, MC

**Department:** Surgery/Urology      **Facility:** MAMC

**Associate Investigator(s):** LTC Henry E. Ruiz, MC; MAJ J. Brantley Thrasher, MC; CPT Douglas W. Soderdahl, MC; MAJ John B. Ellsworth, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC

**Keywords:** Penile Prosthesis: Ambicor, Inflatable, Safety, Effectiveness

**Start Date:**  
8/16/1996

**Est. Completion Date:**  
Oct 02

**Periodic Review:**  
8/27/2002

**Study Objective:** The primary effectiveness objective is to evaluate the ability of the AMS Ambicor inflatable penile prosthesis to provide an erection suitable for sexual intercourse (device function) as determined by physical examination and patient self-report. Secondary effectiveness objectives include estimating the effects of the prosthesis on patient sexual function and satisfaction, self-esteem, quality of life, and psychological well-being. The study will also evaluate levels of patient satisfaction with various aspects of the prosthesis including rigidity, length, girth and flaccidity. Safety will be evaluated by measuring rates of post implant complications (including device malfunction) and the occurrence of medical conditions.

**Technical Approach:** This is a multi-center, prospective, cohort study with the pre-implant experience of patients serving as the comparison for the evaluation of effectiveness and safety. The study sample will be derived from patients who present to the clinic with the diagnosis of erectile dysfunction. After an eligible patient makes an informed decision to be implanted with an AMS Ambicor penile prosthesis and signs the surgical consent he will be asked to participate in the study. A total of 250 patients will be recruited nationwide (12-20 being from MAMC) and will be implanted with the Ambicor inflatable penile prosthesis. The primary measure of effectiveness (sexual function, self-esteem, and psychological well-being), will be monitored for 2 years with visits at 6 weeks post-surgery, 6 months, 1 year, 18 months and 2 years. Follow-up for complications, associated medical conditions and other adverse device effects will be followed for 5 years with phone contact at 3 and 4 years, and a visit at 5 years.

**Progress:** A total of 47 patients have enrolled in this study at MAMC, with 9 patients enrolled during FY02. A request to allow MAMC to enroll 10 additional patients was approved by the IRB, Jan 02. Patient follow-up continues.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 99/089                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> Phase III Randomized, Double-Blind Study of DFMO vs. Placebo in Low Grade Superficial Bladder Cancer   |  |                                      |
| <b>Principal Investigator:</b> COL Raymond A. Costabile, MC  |  |                                      |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> LTC Robert C. Allen, MC; MAJ Bryon D. Joyner, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C. Evans, MC; MAJ Andrew C. Peterson, MC; LTC Henry E. Ruiz, MC; MAJ Thomas L. Poulton, MC  |  |                                      |
| <b>Keywords:</b> Cancer: bladder, DFMO   |  |                                      |
| <b>Start Date:</b><br>8/24/1999  | <b>Est. Completion Date:</b><br>Mar 03 | <b>Periodic Review:</b><br>6/25/2002 |
| <b>Study Objective:</b> To compare DFMO to placebo in patients with low grade superficial bladder cancers according to a) time to first recurrence of tumor, and b) toxicities.  |  |                                      |
| <b>Technical Approach:</b> This will be a phase III randomized, double blind study of DFMO (an inhibitor of ornithine decarboxylase) versus placebo in low-grade superficial bladder cancers. Patients who meet the eligibility criteria will be stratified according to 1) history of newly diagnosed vs. recurrent; 2) stage Ta vs. T1; 3) grade 1 vs. grade 2; and 4) multifocal vs unifocal tumors. Then patients will be centrally randomized to receive either DFMO 1 gm/day or placebo, orally for 12 months in a double-blind fashion. Treatment will be discontinued in the presence of biopsy-proven recurrent disease, unacceptable toxicity, or patient refusal; however, every effort will be made to continue follow-up on these patients until the end of study. Patients will be followed with cystoscopy every three months for 2 years (every 6 months the 3rd year and annually for the 4th year). Based on 1.5 year enrollment and 3 year follow-up, study duration will be 5.5 years. CBC, including platelet count will be required within 12 weeks of randomization and at 6 months. An audiogram will be required at baseline and when indicated during the study. An independent pathologist will centrally review tumor specimens. |  |                                      |
| <b>Progress:</b> A total of 9 patients have been consented into this study with no patients enrolled during FY02. Two of these patients withdrew their consent prior to receiving the implant and the remaining 7 are still being followed.  |  |                                      |

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/028 | <b>Status:</b> Ongoing |
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**Title:** Prospective, Randomized, Double-Blind, Placebo-Controlled Evaluation of Topical Alprostadil Administered at Home for the Treatment of Women with Female Sexual Arousal Disorder

**Principal Investigator:** COL Raymond A. Costabile, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL Gary D. Davis, MC; LCDR Amy L. O'Boyle, MC, USNR; LTC Robert C. Allen, MC; CPT Leah P. McMann, MC; MAJ Andrew C. Peterson, MC; LTC Henry E. Ruiz, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Jack R. Walter, MC

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**Keywords:** FSAD, female sexual arousal disorder

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**Start Date:**  
1/22/2002

**Est. Completion Date:**  
Feb 03

**Periodic Review:**

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**Study Objective:** To provide safety and efficacy data on the use of topically applied alprostadil (PGE) for the treatment of DSM-IV female sexual arousal disorder.

**Technical Approach:** Following a one month lead-in period, subjects will receive two months of blinded home treatment. The first dose of solution will be self-administered in the clinic. Subject will be monitored for adverse events for two hours. For at-home use, subject will apply the solution around genitalia prior to sexual activity. Efficacy of the solution will be measured through subject responses in an event log. Additionally, subjects will fill out questionnaires as to overall satisfaction with the treatment.

**Progress:** During FY02, a total of 17 patients were enrolled at MAMC. One patient withdrew consent, one patient was a screen failure and 11 have received and completed the study treatment. 3 patients are in screening and one patient is still being followed. Patient follow-up will continue for FY03. Enrollment remains ongoing.



### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/118                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Prospective, Double-blinded, Randomized, Crossover Study Comparing the Current Method for Inserting Transurethral Alprostadil (MUSE) with Insertion Following an Application of Either KY or 2% Lidocaine Jelly |  |                         |
| <b>Principal Investigator:</b> CPT Brian J. DeCastro, MC  |  |                         |
| <b>Department:</b> Surgery/Urology  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> COL Raymond A. Costabile, MC  |  |                         |
| <b>Keywords:</b> Erectile dysfunction, MUSE, lidocaine, transurethral alprostadil   |  |                         |
| <b>Start Date:</b><br>9/24/2002   | <b>Est. Completion Date:</b><br>Sep 03 | <b>Periodic Review:</b> |

**Study Objective:** To show if the use of KY Jelly or 2% Lidocaine Jelly prior to insertion of transurethral Alprostadil is effective in increasing compliance and satisfaction by decreasing the painful side effects associated with its use. To demonstrate that the KY jelly or lidocaine jelly does not have any impact on the efficacy of the drug or on the sensitivity of the penis

**Technical Approach:** This study will be broken into three phases. In the first phase patients will be consented and all patients will insert the MUSE tablet as it is currently prescribed without using lubrication. All patients will use MUSE to standard of care without lubrication for 4 weeks. After each use they will fill out an IIEF questionnaire and use-diary with a pain scale to act as a baseline. Throughout each phase patients will be encouraged to use MUSE at least once a week. In the second phase, the patients will be randomized into two groups. One group will receive Xylocaine 2% while the other group will receive KY jelly for 4 weeks. Five minutes prior to the insertion of the MUSE pellet, 3 ml of jelly will be inserted into the distal urethra using a 3 ml syringe. The pellet will then be inserted in the standard fashion with the polypropylene applicator. Again, after each use the patients will be required to fill out IIEF questionnaire and a use-diary with a pain scale. In the third phase both groups will get the opposite jelly and use it as previously described. After each use they will again fill out the IIEF questionnaire and diary.

**Progress:** This protocol received IRB approval late in FY02 and has not yet begun.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 99/003 | <b>Status:</b> Completed |
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**Title:** A Randomized Double-Blind Comparative Trial of Bicalutamide (CASODEX) 150 mg Monotherapy Versus Placebo in Patients with a Rising PSA After Radical Prostatectomy for Prostate Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** COL John M. Bauman, MC; COL Marc G. Cote, MC; Jerome Billingsley, M.D.; James H. Timmons, MD; MAJ Sunil K. Ahuja, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C. Evans, MC; MAJ Andrew C. Peterson, MC

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**Keywords:** Bicalutamide, PSA, Prostatectomy, Cancer:Prostate

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**Start Date:**  
10/20/1998

**Est. Completion Date:**  
Jan 01

**Periodic Review:**

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**Study Objective:** (1) To compare bicalutamide 150 mg with placebo for time to treatment failure; (2) Quality of Life.

**Technical Approach:** Subjects will be randomized to receive either bicalutamide 150 mg daily or placebo until treatment failure, which is defined as an adverse event leading to withdrawal of randomized therapy, objective disease progression, death, initiation of systemic treatment or radiotherapy, or withdrawal from study therapy for any reason. Quality of Life data includes a PSA anxiety questionnaire (MAX-PC) and the FACT-P instrument, time to objective disease progression, PSA response, and time to PSA progression.

**Progress:** A total of 17 patients enrolled in this study at MAMC. Thirteen patients received study treatment, three patients withdrew prior to screening or receiving study drug and one patient was a screen failure. One patient died; however this death was considered unrelated to study participation. All patient follow-up visits were completed prior to FY02. The study was reported as permanently closed at MAMC, 26 Feb 02.

### Detail Summary Sheet

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|---|--|-------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 202/046                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Randomized Trial of Radical Prostatectomy versus Brachytherapy for Patients with T1c or T2a N0 M0 Prostate Cancer |  |                         |
| <b>Principal Investigator:</b> MAJ Raymond S. Lance, MC   |  |                         |
| <b>Department:</b> Surgery/Urology  |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> COL Raymond A. Costabile, MC; LTC William B. Reece, MC; LTC John B. Halligan, MC                |  |                         |
| <b>Keywords:</b> TRUS - transrectal ultrasound of prostate, prostate specific antigens PSA  |  |                         |
| <b>Start Date:</b><br>2/26/2002   | <b>Est. Completion Date:</b><br>Mar 07 | <b>Periodic Review:</b> |

**Study Objective:** To ascertain whether patients assigned to receive brachytherapy have equal or better overall survival as compared to patients randomized to receive radical prostatectomy. Also, to compare the two treatment arms with respect to metastasis-free survival, probability of survival without symptoms, side effects from the intervention, and quality of life, addressed in companion study.

**Technical Approach:** Subjects will be randomized, with equal probability to either Arm 1: Radical Prostatectomy (RP) followed by appropriate secondary interventions at failure, or Arm 2: Brachytherapy (BT) followed by appropriate secondary interventions at failure. All subjects will be followed at months 18, 24, 30, 36, 42, 48, 54, 60, and yearly for survival status until death.

**Progress:** This study has not yet been initiated at MAMC.

### Detail Summary Sheet

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|------------------------|-----------------------|---------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 98/114 | <b>Status:</b> Terminated |
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**Title:** A Uniformed Services Comprehensive Database and Tissue Repository for the Study of Epidemiological, Detection, Natural History, and New Management Strategies for Prostate Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC Stephen C. Groo, MC

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**Keywords:** Cancer:prostate, database, tissue repository

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**Start Date:**

9/15/1998

**Est. Completion Date:**

Jun 03

**Periodic Review:**

7/15/2002

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**Study Objective:** To establish a prostate cancer serum and tissue repository that will focus on the pathology and contain supportive clinical data for the study of the etiology of prostate cancer and will incorporate a demonstration project to illustrate the utility of the repository by examining interracial differences among men with prostate cancer.

**Technical Approach:** Subjects will be asked to allow the intraoperative collection of a blood sample, tissue biopsies of the excised organ and use of these specimens, as well as the retrieval and use of their original archival biopsy tissue. The sera and tissue will be tested for new markers in later studies to be conducted by both military and civilian prostate cancer researchers. Some of serum and tissue may be supplied to other research centers in the future.

**Progress:** This study was terminated by principal investigator, effective 15 Jul 02, prior to its initiation at MAMC.

### Detail Summary Sheet

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|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/090                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> An Open-Label Trial on the Effect of I.V. Zometa 4 mg on Bone Mineral Density in Hormone Sensitive Prostate Cancer Patients with Bone Metastasis, Protocol Number CZOL446EUS24   |  |                         |
| <b>Principal Investigator:</b> MAJ Raymond S. Lance, MC  |  |                         |
| <b>Department:</b> Surgery/Urology   |  | <b>Facility:</b> MAMC   |
| <b>Associate Investigator(s):</b> COL Raymond A. Costabile, MC; LTC Robert C. Allen, MC; CPT Leah P. McMann, MC; MAJ Andrew C. Peterson, MC  |  |                         |
| <b>Keywords:</b> zoledronate electrocardiogram bone density hormone sensitive prostate cancer  |  |                         |
| <b>Start Date:</b><br>6/25/2002  | <b>Est. Completion Date:</b><br>Aug 04 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> The primary objective of this study is to determine the effect of 12 months of intravenous Zometa (zolderonic acid) 4 mg on bone mineral density (BMD), specifically in the lumbar spine, in prostate cancer patients with a history of metastatic bone disease who are concurrently receiving hormonal therapy. This study has secondary objectives to identify changes in biochemical markers of bone formation, to determine the effect on BMD in the total hip, to determine the time to the first occurrence of a skeletal-related event (SRE), and to assess the safety of Zometa 4 mg every 3 weeks in this patient population. |  |                         |
| <b>Technical Approach:</b> Subjects meeting study criteria will be given 16 infusions of the study drug. Before and after the treatment, subjects wil have a DEXA scan to determine bone mineral density.  |  |                         |
| <b>Progress:</b> No patients have been enrolled into this study during FY02.   |  |                         |

### Detail Summary Sheet

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|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/140 | <b>Status:</b> Ongoing |
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**Title:** Intratumoral Treatment of Human Prostate Cancer Xenografts by Polymeric Gel Delivery of Yttrium-90 with and without Taxol

**Principal Investigator:** MAJ Raymond S. Lance, MC

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| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
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**Associate Investigator(s):** LTC John B. Halligan, MC; LTC William B. Reece, MC; CPT Jack R. Walter, MC

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**Keywords:** Cancer, polymer, tumor, mouse

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**Start Date:**

9/24/2001

**Est. Completion Date:**

Sep 04

**Periodic Review:**

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**Study Objective:** We hypothesize that intratumoral injection with polymeric gel containing cytotoxic chemo- and/or radiotherapeutic agent(s) will result in tumoricidal activity against human prostate xenografts without significant migration to other body tissues or fluids.

**Technical Approach:** 6-8 week old male nude mice will be injected, subcutaneously, in the upper back with  $2 \times 10^6$  LnCap cells (the only human prostate cancer cell line that is androgen sensitive, thus better reflecting clinically localized prostate cancer) in 0.1-0.2 cc suspensions. Mice will be randomly assigned to specific control/treatment groups at the time of cancer cell injection. Tumors will grow to 6-10 mm in diameter over approximately 4-6 weeks, at which time control or treatment intervention will be applied as described below. A control group of 5 mice will have no therapy applied. 5 other control mice will receive intratumoral injections with the polymeric compound alone. Treatment group Ia will consist of 15 mice receiving intratumoral injection of polymeric gel plus Yttrium-90. Treatment group Ib will include 15 mice receiving intratumoral injections of Yttrium-90 alone (no polymeric gel). Treatment group IIa will include 10 mice subjected to intratumoral injection of polymeric gel combined with Yttrium-90 and Taxol. Treatment group IIb will include 10 mice receiving intratumoral injection with yttrium-90 plus Taxol alone (no gel). Treatment group IIIa will have 10 mice getting intratumoral injection with Taxol in the polymeric gel. Finally, treatment group IIIb will receive intratumoral injection with taxol alone (no polymeric gel). The treatment injection volume will be standardized between and within treatment groups, and will not exceed 0.1 cc. Five animals each, in treatment groups Ia and Ib will euthanized 5 days following intratumoral injections of yttrium-90 in order to measure for systemic radiation (bioavailability/ biodistribution). Lungs, liver, kidneys, blood, urine and colonic feces will be harvested and tested with a beta counter.

**Progress:** The protocol has been completed with the exception being the final pathologic evaluation of mouse tumors. The data presently indicates that the use of the polymeric gel did not add any therapeutic benefit over saline in the use of intratumoral injections of Yttrium-90 with or without Taxol. This novel anti-cancer proof of principal study while it did not result in the eradication of any of the human prostate cancers, did demonstrate that this approach can be used safely. Furthermore, a great deal of knowledge about this very unique treatment approach, ie intratumoral injection, was gained and will provide substrate for further experiments.

### Detail Summary Sheet

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| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 98/092                  | <b>Status:</b> Ongoing               |
| <b>Title:</b> Multicenter Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analysis  |  |                                      |
| <b>Principal Investigator:</b> MAJ Raymond S. Lance, MC  |  |                                      |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                                      |
| <b>Associate Investigator(s):</b> COL Raymond A. Costabile, MC; MAJ J. Brantley Thrasher, MC; CPT Jack R. Walter, MC; Karen E. Smith, M.D.; John P. Murphy, M.D.   |  |                                      |
| <b>Keywords:</b> Cancer;prostate, data base, patterns of care, prognostic factors, long-term outcomes  |  |                                      |
| <b>Start Date:</b><br>7/17/1998  | <b>Est. Completion Date:</b><br>Jan 13 | <b>Periodic Review:</b><br>6/18/2002 |
| <b>Study Objective:</b> Comprehensive longitudinal collection, maintenance and analysis of prostate cancer-specific and demographic standardized information from a large cohort of military health care beneficiaries from multiple geographically diverse health care centers.   |  |                                      |
| <b>Technical Approach:</b> Standardized data collection instruments will be used at ten military medical centers by clinical research personnel and physicians to collect comprehensive prospective and retrospective information from men with prostate cancer . Patients will be followed proactively at a minimum of every twelve months until death. Data will be entered and maintained securely at USUHS in a relational database designed exclusively for this purpose. Standard statistical analysis will include survival analysis and univariate and multivariate analysis for prognostic factors. |  |                                      |
| <b>Progress:</b> During FY02, 197 subjects were enrolled into the database, for a MAMC total of 1659 patients. Study enrollment continues.   |  |                                      |

### Detail Summary Sheet

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|                        |                       |                        |
|------------------------|-----------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 94/010 | <b>Status:</b> Ongoing |
|------------------------|-----------------------|------------------------|

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**Title:** SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup

**Principal Investigator:** MAJ Raymond S. Lance, MC

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|                                    |                       |
|------------------------------------|-----------------------|
| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
|------------------------------------|-----------------------|

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**Associate Investigator(s):** COL Raymond A. Costabile, MC; MAJ J. Brantley Thrasher, MC; MAJ Rajat Bannerji, MC

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**Keywords:** Cancer: prostate, Finasteride

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**Start Date:**

10/1/1993

**Est. Completion Date:**

Nov 03

**Periodic Review:**

8/27/2002

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**Study Objective:** The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

**Technical Approach:** Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

**Progress:** This protocol closed to patient entry, 1 Jan 97. Total MAMC patients consented 101; patients with incomplete enrollment (i.e., did not receive study drug due to elevated PSA, etc) 18; patients voluntarily withdrawn 23, and patients transferred to another institution 2. Total number of patients continuing on active protocol during FY02 is 58.



### Detail Summary Sheet

|  |  |                         |
|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/122                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> Followup of Testicular Microlithiasis in an Asymptomatic Population  |  |                         |
| <b>Principal Investigator:</b> CPT Leah P. McMann, MC  |  |                         |
| <b>Department:</b> Surgery/Urology   | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> CPT Frederick L. Stephens II, MC; COL Raymond A. Costabile, MC; MAJ Andrew C. Peterson, MC |  |                         |
| <b>Keywords:</b> testis lithiasis testicular neoplasms ultrasonography   |  |                         |
| <b>Start Date:</b><br>9/24/2002  | <b>Est. Completion Date:</b><br>Dec 02 | <b>Periodic Review:</b> |

**Study Objective:** To determine the incidence of testis tumor at two, five, and ten-year followup in the 84 men previously identified with testicular microlithiasis in the original study by Peterson et al. entitled The Prevalence Of Testicular Microlithiasis in an Asymptomatic Screening Population.

**Technical Approach:** Patients will be identified through the data collected at ROTC Advance Camp 2000. All patients identified with TM will be contacted by telephone. If they agree to participate, the study investigator will administer a telephonic questionnaire on year 2002, 2005, and 2010.

**Progress:** Protocol just received approval. Work has not yet begun on this protocol.

### Detail Summary Sheet

|                        |                        |                        |
|------------------------|------------------------|------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 202/065 | <b>Status:</b> Ongoing |
|------------------------|------------------------|------------------------|

**Title:** Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial

**Principal Investigator:** CPT Leah P. McMann, MC

|                                    |                       |
|------------------------------------|-----------------------|
| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
|------------------------------------|-----------------------|

**Associate Investigator(s):** MAJ Andrew C. Peterson, MC; COL Raymond A. Costabile, MC

**Keywords:** penis surgery therapy ketoconazole impotence

**Start Date:**  
4/23/2002

**Est. Completion Date:**  
Dec 02

**Periodic Review:**

**Study Objective:** To determine if ketoconazole adequately prevents penile erections after penile surgery

**Technical Approach:** This study will be broken into three phases. Phase 1-Patients will be identified in the urology clinic who are scheduled to undergo penile or urethral surgery. Prior to surgery, they will be offered participation and randomized to receive ketoconazole or placebo. Forty patients will be randomized in a 1:1 ratio to ketoconazole or placebo. Phase 2-Forty-eight hours before surgery, the patient will be started on the study drug (ketoconazole 400 mg or placebo TID for a total treatment period of ten days). They will be administered the study questionnaire to fill out at the end of the treatment period. Phase 3- A follow-up telephone call will be made six weeks postoperatively to assess patient satisfaction with the outcome of surgery.

**Progress:** Ongoing enrollment. I have been working with pharmacy to make the keto and placebo and have been recruiting patients. Since enrollment started in June 02, we have enrolled 12 but 3 dropped out due to decision by the patient to postpone or cancel surgery.

### Detail Summary Sheet

|   |  |                                       |
|---|--|---------------------------------------|
| <b>Date:</b> 30 Sep 02  | <b>Number:</b> 201/069                 | <b>Status:</b> Ongoing                |
| <b>Title:</b> Outcome After Ureteral Reimplantation: A Comparison of Extravesical Versus Intravesical Techniques, A Retrospective Study |  |                                       |
| <b>Principal Investigator:</b> CPT Leah P. McMann, MC   |  |                                       |
| <b>Department:</b> Surgery/Urology  | <b>Facility:</b> MAMC                  |                                       |
| <b>Associate Investigator(s):</b> MAJ Bryon D. Joyner, MC   |  |                                       |
| <b>Keywords:</b> vesico-ureteral reflux, ureteroneocystostomy, ureter   |  |                                       |
| <b>Start Date:</b><br>2/27/2001   | <b>Est. Completion Date:</b><br>Jun 01 | <b>Periodic Review:</b><br>12/18/2001 |

**Study Objective:** The purpose of our study is to compare outcomes with respect to obstruction, resolution of reflux, and length of hospital stay after extravesical versus intravesical ureteral reimplantation at this institution.

**Technical Approach:** This is a retrospective chart review to compare outcomes of the extravesical versus intravesical techniques in surgically treating vesicoureteral reflux. This is an effort to determine if one approach is superior to the other in terms of outcome and complication rate at this institution. The sample size of 48 represents those patients who met the inclusion criteria for entrance into the study, namely documentation of vesicoureteral reflux as a primary diagnosis and underwent ureteral reimplantation between 1996 and 2000. If one method is found clearly superior over the other in terms of fewer complications and shorter hospital stay, it may influence the decision of which technique to use in future reimplantations.

**Progress:** Approximately 60 patients were identified. After a chart review of ureteral reimplantations done at MAMC in a five year period, we compared outcomes of extravesical and intravesical reimplantation and found that resolution of hydronephrosis and reflux were similar (>90%), but length of stay and hence cost was less with extravesical versus intravesical reimplantation.

### Detail Summary Sheet

|                        |                        |                          |
|------------------------|------------------------|--------------------------|
| <b>Date:</b> 30 Sep 02 | <b>Number:</b> 201/066 | <b>Status:</b> Completed |
|------------------------|------------------------|--------------------------|

**Title:** Significance of Soluble Fas in the Serum of Patients with Prostate Cancer

**Principal Investigator:** CPT Leah P. McMann, MC

|                                    |                       |
|------------------------------------|-----------------------|
| <b>Department:</b> Surgery/Urology | <b>Facility:</b> MAMC |
|------------------------------------|-----------------------|

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; COL Raymond A. Costabile, MC

**Keywords:** prostate cancer, Fas, sFas, prognosis, serum markers

**Start Date:**  
2/27/2001

**Est. Completion Date:**  
Mar 02

**Periodic Review:**  
12/18/2001

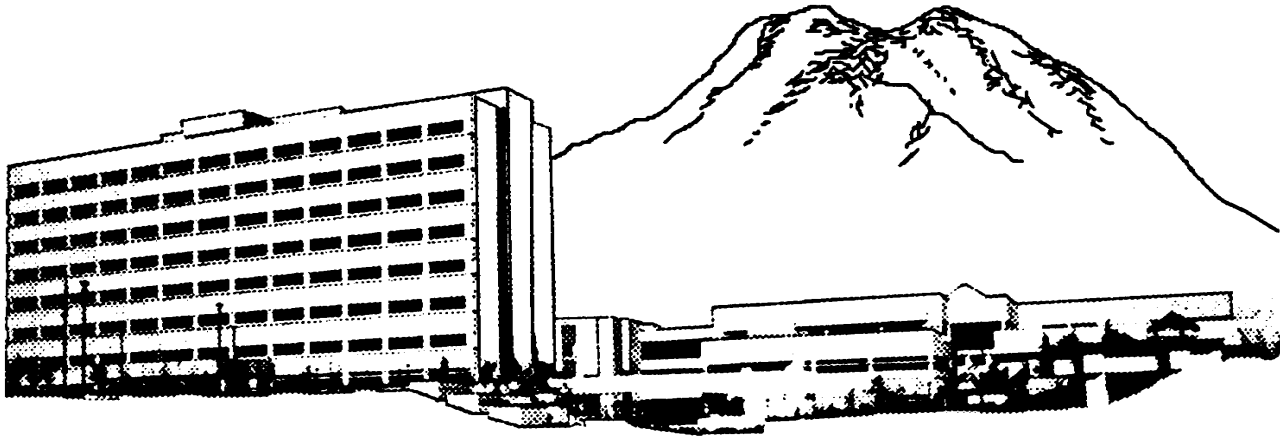
**Study Objective:** To determine the level of soluble Fas (sFas) in serum of patients with and without metastatic prostate.

**Technical Approach:** Elevated serum sFas levels have been shown in hematopoietic and nonhematopoietic malignancies. However, sFas levels in the serum of prostate cancer patients have not been reported in the literature. Serum sFas level may prove to be a useful prognostic indicator for prostate cancer if it is found to correlate with tumor stage and/or grade as well as disease-specific survival rate and post-treatment disease-free interval. The goal of this study is to investigate the utility of serum sFas levels as a biomarker for malignant potential in human prostate cancer. Specifically, we will compare sFas levels in the serum of 20 patients without prostate cancer and 20 patients with benign prostatic hyperplasia with patients who have locally confined (20 patients) or confirmed metastatic (20 patients) prostate cancer and correlate these levels with tumor stage and grade. In addition, we will compare serum sFas levels in the subgroup of locally confined prostate cancer patients before and after definitive treatment with either radical prostatectomy, external beam radiation, or brachytherapy. Serum sFas levels will be quantified using a Fas-specific enzyme-linked immunosorbent assay.

**Progress:** During FY 2001, we finished the protocol. We ran ELISAs on sera from men with localized cancer, biochemical failures, and metastatic disease and compared the sFas levels with those of men without prostate cancer. We found no difference in mean sFas levels between men without cancer, and men with advanced prostate cancer, but found that mean sFas levels dropped in men with localized cancer. Perhaps this is due to some upregulation of the immune system in the early states of prostate cancer, but when the cancer becomes more aggressive or recurs, it overcomes immune surveillance and is able to metastasize. This will be presented at the AUA western section in Oct 02.

## Detail Summary Sheet

|   |  |  |  |                                      |  |
|---|--|--|--|--------------------------------------|--|
| <b>Date:</b> 30 Sep 02  |  | <b>Number:</b> 200/060                 |  | <b>Status:</b> Completed             |  |
| <b>Title:</b> The Effect of 1,25-dihydroxyvitamin D3 (vitamin D) on Vascular Endothelial Growth Factor (VEGF) mRNA and Protein Expression in Prostate and Bladder Cancer Cell Lines   |  |  |  |                                      |  |
| <b>Principal Investigator:</b> MAJ Thomas L. Poulton, MC  |  |  |  |                                      |  |
| <b>Department:</b> Surgery/Urology  |  |  |  | <b>Facility:</b> MAMC                |  |
| <b>Associate Investigator(s):</b> Lisa M. Pierce, D.Sc.; COL Raymond A. Costabile, MC   |  |  |  |                                      |  |
| <b>Keywords:</b> vascular endothelial growth factor, VEGF, prostate cancer, bladder cancer, vitamin D, telomerase   |  |  |  |                                      |  |
| <b>Start Date:</b><br>4/25/2000   |  | <b>Est. Completion Date:</b><br>Apr 01 |  | <b>Periodic Review:</b><br>3/27/2001 |  |
| <b>Study Objective:</b> To determine the effect of varying concentrations of 1,25-dihydroxyvitaminD3 (Vitamin D) on the expression of vascular endothelial growth factor (VEGF) mRNA and protein in prostate and bladder cancer cell lines in vitro. In addition, we will determine the effect of vitamin D exposure on telomerase activity in these prostate and bladder cancer cell lines.  |  |  |  |                                      |  |
| <b>Technical Approach:</b> Cell Culture: The human prostate cancer cell line LNCaP and M12 and the human bladder cancer cell line T24 will be used for analysis in this study. After the cells reach confluency in their appropriate medias, the media will be replaced with fresh media containing either vehicle (0.1% ethanol) or various concentrations of 1,25-dihydroxyvitamin D3 for various times. The cells then will be processed for RNA extraction/Northern Analysis and for protein extraction/Western Analysis. The cells will also be extracted for telomerase activity. Northern Analysis: After total RNA extraction, the RNA will be resoved on a 0.8% agarose-formaldehyde ge transferred to a Nytran filter and UV cross-linked to the membrane . After prehybridization, hybridization with probes of complementary DNAs for VEGF and 18S RNA will be carried out. Labeling will involve the use of alpha 32P dCTP and measurement is involve densitometry relative to VEGF mRNA present in the samples. Western Analysis: 30 uG of total protein lysates will be denatured and boiled prior to loading on a 12% polyacrylamide gell with a 5% stacking gel and transferred overnight onto a polyvinylidene difluoride membrane. After blocking, the membrane will be probed using a rabbit polyclonal anti-human VEGF antibody, and probed again with a mouse anti-glyceraldehyde-3phosphate dehydrogenase (GAPDH) antibody. The secondary will be a peroxidase-conjugated anti-mouse IgG antibody. Detection will be determined by densitometry using chemiluminescence. Telomerase Activity: Telomerase acitvey will be measured on prostate and bladder cancer cell lines using a commercially available kit (Telomerase PCR ELISA) following manufactureres (Boehringer Mannheim) instructions. |  |  |  |                                      |  |
| <b>Progress:</b> All work on this bench study has been completed. Two prostate cancer cell lines (LNCaP, M12) and a bladder cancer cell line (T24) were grown to confluency, serum starved for 48 hours, and exposed to various concentrations of 1,25 dihydroxyvitamin D3 (0, 10, 100 nM). At 2 days and 3 days of vitamin D exposure, supernatants were collected and cells were harvested and counted. VEGF secreted into the media was measured by enzyme linked immunosorbent assay. Telomerase activity was measured in the cells using the Telomerase Repeat Amplification Protocol. Results: All three cell lines secreted VEGF protein into the media, although M12 cells produced less VEGF than LNCaP cells (p<0.05; student t test) and T24 cells (p<0.05 student t test). In vitro vitamin D exposure did not reduce VEGF production in any of the prostate or bladder cancer cell lines. In addition, vitamin D did not decrease telomerase activity in any cell line. Conclusions: The anticarcinogenic effects of vitamin D do not appear to include downregulation of VEGF protein expression and telomerase activity in prostate and bladder cancer.  |  |  |  |                                      |  |

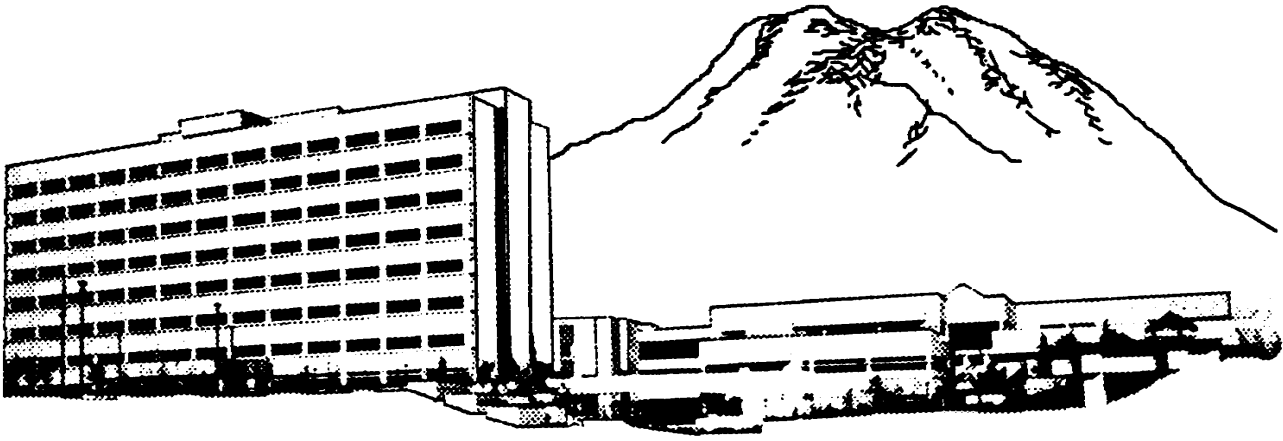


## **Detail Summary Sheets**

### **Vascular Surgery, Department of Surgery**

### Detail Summary Sheet

|  |  |                         |
|--|--|-------------------------|
| <b>Date:</b> 30 Sep 02   | <b>Number:</b> 202/070                 | <b>Status:</b> Ongoing  |
| <b>Title:</b> A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy with Split-Thickness Skin Grafting in the Treatment and Blinded Evaluation of Venous Stasis Ulcers, Protocol Number VAC2001-03  |  |                         |
| <b>Principal Investigator:</b> Charles A. Andersen, M.D.   |  |                         |
| <b>Department:</b> Surgery/Vascular Surgery  | <b>Facility:</b> MAMC                  |                         |
| <b>Associate Investigator(s):</b> LTC Neal C. Hadro, MC; Mary Anne Landowski, RN; Vickie R. Driver, DPM  |  |                         |
| <b>Keywords:</b> ankle brachial index vacuum closure skin graft  |  |                         |
| <b>Start Date:</b><br>5/28/2002  | <b>Est. Completion Date:</b><br>Jul 04 | <b>Periodic Review:</b> |
| <b>Study Objective:</b> The primary objectives of this study are the facilitation of surgical closure and a successful graft take at 90 days. The secondary objectives are a reduction in recurrence, a reduction in required operating room time, a reduction in complications, pain reduction, improved quality of life and a reduction in average total cost of care.   |  |                         |
| <b>Technical Approach:</b> This study will be looking at approximately 10 males or females 18 years of age or older that have venous stasis ulcers >30 days duration and >25cm <sup>2</sup> in area. Study participants will be randomized to receive either standard of care or treatment with vacuum assisted closure therapy. Subjects will be monitored to see if using the vacuum assisted closure device facilitates surgical closure of the ulcer and successful graft take at 90 days. Results from using the vacuum device will be compared to results from using standard of care. |  |                         |
| <b>Progress:</b> This study has not yet begun at MAMC.   |  |                         |



## **Detail Summary Sheets**

# **Weed Army Community Hospital**



## Detail Summary Sheet

**Date:** 30 Sep 02

**Number:** 202/104

**Status:** Ongoing

**Title:** Coccidioidomycosis Seroincidence Study

**Principal Investigator:** MAJ Mark B. Potter, MC

**Department:** Weed Army Community Hospital

**Facility:** MAMC

**Associate Investigator(s):** LCDR Nancy Crum, MC, USNR; CPT Mark Wallace, MC; MAJ Nina Karlin, MC; CDR Braden Hale, MC, USN; CDR Margaret A. K. Ryan, MC, USN; CDR Kevin Russell, MC, USN; CDR Gregory Utz, MC, USN

**Keywords:** coccidioidomycosis valley fever seroincidence C.immitis infection

**Start Date:**  
8/27/2002

**Est. Completion Date:**  
Sep 02

**Periodic Review:**

**Study Objective:** To determine the seroincidence of coccidiomycosis (cases of new infections) in a group of military trainees participating in a typical 5-week exercise at Ft. Irwin.

**Technical Approach:** This study will be conducted to determine the seroincidence of coccidiomycosis, a fungal disease endemic to the desert areas of the Southwest U.S. This study will determine seroincidence by two blood draws, one at the beginning of training and the second after the completion of the 5-week training exercise. The population will be Army trainees who are performing military exercises at Ft Irwin in August-September of 2002. The study will be a prospective cohort study to determine the seroincidence of coccidiomycosis among military trainees. Enrollment will be offered to each trainee by the study protocol personnel without involvement of the trainees' chain of command (NCO or officers). An ombudsman, not connected in any way with the proposed research or the unit, shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate. All trainees enrolling for the training exercise at Ft. Irwin will be asked to participate and up to 400 of the trainees will be enrolled. Each enrollee will sign an informed consent, provide demographic and travel/medical history, and donate 10cc of blood before and after the training exercise for coccidiomycosis testing. At the end of the training, each enrollee will report any symptoms that have developed during training and blood for a repeat coccidiomycosis serology. We will determine the number of trainees who develop C.immitis infection. Those who develop coccidiomycosis will be compared to non-cases in terms of potential risk factors between these groups including age, sex, race, rank, and medical conditions.

**Progress:** 379 subjects were entered into this study during FY02. To date we have had 3 confirmed positive results. What we mean by that is they were negative for the coccidiomycosis antibody at their first blood draw and positive at their second blood indicating they have been exposed and infected. We also have several indeterminant results (31 soldiers had indeterminant results). These indeterminant results may represent early infection. For these indeterminant results we are checking a 3rd sample and are in the process of notifying these soldiers to get their blood drawn again. These soldiers with positive or indeterminant results will also have an H&P and a chest xray if indicated. Any soldier with a positive confirmatory test with symptoms or positive chest xray will receive the necessary chemotherapy.

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